

A poetic understatement

The actual number is in the billions. For more than 15 years, Dalmane (flurazepam HCI/Roche) has been providing sleep that satisfies patients—sleep that comes quickly and lasts through the night."

Sleep that satisfies *you*—you can count on an exceptionally wide margin of safety. As always, caution patients about driving or drinking alcohol.



DALMANE

flurazepam HCI/Roche ® sleep that satisfies

References: 1. Kales J, et al: Clin Pharmacol Ther 12:691-697, Jul-Aug 1971. 2. Kales A, et al: Clin Pharmacol Ther 18:356-363, Sep 1975. 3. Kales A, et al: Clin Pharmacol Ther 19:576-583, May 1976. 4. Kales A, et al: Clin Pharmacol Ther 19:576-583, May 1976. 4. Kales A, et al: Clin Pharmacol Ther 32:781-788, Dec 1982. 5. Frost JD Jr, DeLucchi MR: J Am Geriatr Soc 27:541-546, Dec 1979. 6. Dement WC, et al: Behav Med, pp. 25-31, Oct 1978. 7. Kales A, Kales JD: J Clin Psychopharmacol 3:140-150, Apr 1983. 8. Tennant FS, et al: Symposium on the Treatment of Sleep Disorders, Teleconference, Oct 16, 1984. 9. Greenblott DJ, Allen MD, Shader RI: Clin Pharmacol Ther 21:355-361, Mar 1977.

DALMANE®

flurazepam HCI/Roche @ sleep that satisfies

15-ma/30-ma capsules

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; in acute or chronic medical situations requiring restful sleep. Objective sleep laboratory data have shown effectiveness for at least 28 consecutive nights of administration. Since insomnia is often transient and intermittent, protonged administration is generally not necessary or recommended. Repeated therapy should only be undertaken with appropriate patient

Contraindications: Known hypersensitivity to flurazepam HCI; pregnancy, Benzodiazepines may cause fetal damage when administered during pregnancy. Several studies suggest an increased risk of congenital malformations associated with benzodiazepine use during the first trimester. Warm patients of the potential risks to the fetus should the possibility of becoming pregnant exist while receiving flurazepam. Instruct patients to discontinue drug prior to becoming pregnant. Consider the possibility of pregnancy prior to instituting therapy.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. An additive effect may occur if alcohol is consumed the day following use for nightlime sedation. This potential may exist for several days following discontinuation. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Potential impairment of performance of such activities may occur the day following ingestion. Not recommended for use in persons under 15 years of age. Withdrawal symptoms rarely reported; abrupt discontinuation should be avoided with gradual tapering of dosage for those patients on medication for a prolonged period of time. Use caution in administering to addiction-prone individuals or those who might increase

Precautions: In elderly and debilitated patients, it is recommended that the dosage be limited to 15 mg to reduce risk of oversedation, dizziness, confusion and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressants. Employ usual precautions in severely depressed patients, or in those with latent depression or suicidal tendencies, or in those with impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported: headache, hearthurn, upset stomach, nausea, vomiting, diarrhea, constipation, Gl pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, prunitus, skin rash, dry mouth, bitler taste, excessive salivation, anorexia, euphoria, depression, sturred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase; and paradoxical reactions, e.g., excitement, stimulation and hyperactivity.

Dosage: Individualize for maximum beneficial effect.

Adults: 30 mg usual dosage; 15 mg may suffice in some patients. Elderly or debilitated patients: 15 mg recommended initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg fluraze-pam HCl.



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WARRING.

HEPATIC FALURE RESULTING IN FATALITIES HAS OCCURRED IN PATIENTS RECEIVING VALPROIC ACID AND ITS DERIVATIVES EXPERIENCE HAS INDICATED THAT CHILDREN UNDER THE AGE OF TWO YEARS ARE AT A CONSIDERABLY INCREASED RISK OF DEVELOPING FATAL HEPATOTOXICITY. ESPECIALLY THOSE ON MULTIPLE ANTEONIVULSANIS, THOSE WITH COMERNTAL META BOLIC DISCRIBES, THOSE WITH SEVERE SELZIVE BOSORDERS ACCOMPANIED BY MENTAL RETARDATION, AND THOSE WITH GAIN OF GANIC BRAIN DESASE, UNEND DEPARTMENT SEVERE SUSED IN THIS PATENT GROUP. IT SHOULD BE USED WITH EXTREME CAUTION AND AS A SOLE AGENT THE BENEFICE OF SEZURE CONTROL. SHOULD BE USED WITH EXTREME CAUTION AND EXPERIENCE HAS INDICATED THAT THE INDICENCE OF FATAL HEPATOTOXICITY DECREASES CONSIDERABLY IN PROBRESSMELY OLDER PATENT GROUP.

THESE INCIDENTS USUALLY HAVE OCCURRED DURING THE FIRST SIX MONTHS OF TREATMENT SERIOUS OR FATAL HEPATOTOXICITY MAY BE PRECEDED BY MOIN SPECIFIC SYMPTOMS SUCH AS LIOSS OF SECURE CONTROL. MALASE, MEANINESS, LETHARDY, FACAL EXCHA. AMOREMA AND YOMITHIS. PATENTS SHOULD BE MONITORED CLOSELY FOR APPARAMENC THESE SYMPTOMS SUCH AS THE THE ATTER. ESPECIALLY DURING THE FIRST SU MONTHS.

DESCRIPTION: Divalgroex sodium is a stable co-ordination compound comprised of sodium valproate and valproic acid in a 1:1 molar relationship and formed during the partial neutralization of valproic acid with 0.5 equivalent of sodium hydroxide. Chemically it is designated as sodium hydrope his (2-posyphenanote).
Divalproex sodium has a molecular weight of 310.41 and occurs as a white powder with a characteristic odor.
DEPAROTE is not antientelized in senteric coated tablets in three dosage strengths containing divalproex sodium equivalent to 125 mg, 250 mg or 500 mg of valproex acid.

Inactive Ingradients
1/2 mg ablest; cellulosis polymers, discreylated monoplycarides, FDAC Blue No. 1, FDAC Red No. 40, povidone, pregelatinized starch (con1/2 mg ablest; cellulosis polymers, discreylated monoplycarides, FDAC Villow No. 6, in on oxide, povidone, pregelatinized starch (con1/2 0m patibatics cellulosis polymers, discreylated monoplycerides, FDAC Villow No. 6, in on oxide, povidone, pregelatinized starch (contains com starch), silica gel. tale, titanium dioxide, vanilian and other ingredients.
500 mg tabletis; cellulosis polymers, discreylated monoplycerides, RDAC Red No. 30, FDAC Blue No. 2 in on oxide, povidone, pregelatinized starch (contains com starch), silica gel. tale, titanium dioxide, vanilian and other ingredients.

Starch (contains com starch), since get, talc, transium dounce, valunium and owner ingrevenents.

CLINICAL PRAMACOLOGY: DPEAVOIT is an antienipletic agent which is chemically related to valproic acid. It has no nitrogen or aromatic moiety characteristic of other antiepiletipic grifty with its chemical problem. The mechanism by which DEPAKOTE exerts its antiepileptic effects has not been established. It has been suggested that its activity is related to increased brain levels of gamma-ammioutryic acid (GABA). The effect on the neuronal membrane is unknown. DEPAKOTE dissociates into valproate in the gastrointestinal tract.

Because of the enteric coating of DPAKOTE, absorption is delayed on thour following onal administration. Thereafter, DEPAKOTE is uniformly and reliably absorbed, as shown by studies in normal volunters. Peak serime levels of valgroate occur in 3 to 4 hours. Biovasiliably in divident to the department of the department of valgroate occur in 3 to 4 hours. Biovasiliably continued to the equivalent to that of DEPAKOTE valgroac acid expassiles. Concentional administration with food woold be expected in love absorption that of DEPAKOTE is uniformly in the start of the continued of the properties of the pr

Enteric-coated divalproex sodium may reduce the incidence of the irritative gastrointesinal effects of valproate as con acid cassules.

acid cappules.

Valoroute is rapidly distributed and at therapeutic drug concentrations, drug is highly bound (90%) to human plasma proteins. Increases in dose may result in decreases in the extent of protein binding and increased valoroute clearance and elimination.

Elimination of DEPAROITE and is neterableise occurs principally in the inner, with moor amounts in the faces and expired air. Very little un-metabolited parent drug is excreted in the uner. The drug is primarily metabolited in the liver and is excreted as the glucuronide conjugate. Dither metabolities in the uner air products of beta, omega i, and mergia outdation (C. S. L. 4 and C. 5 postions). The major conditive metabolities in the uner air products of beta, omega i, and mergia outdation (C. S. L. 4 and C. 5 postions). The major conditive metabolities are 2 propyl-3 bridge relations acid. Indian elimination of the uner air properties of the uner air 2 propyl-3 bridge relations. acid. Indian elimination of the uner air properties and 2 propyl-4 bridge relations acid. Indian elimination of the uner air properties and all 2 propyl-4 bridge relations.

INDICATIONS AND USAGE: DEPAKOTE (divalproex sodium) is indicated for use as sole and adjunctive therapy in the treatment of simple (petit mail) and complex absence seizures. DEPAKOTE may also be used adjunctively in patients with multiple seizure types which in-

simple (petit mail) and complex absence seizures. DEPAKOTE may also be used adjunctively in patients with multiple seizure types which in-clude absence seizures.

In accordance with the International Classification of Seizures, simple absence is defined as very brief clouding of the sensorium or loss of consciousness (lasting usually 2-15 seconds), accompanied by certain generalized piliptic discharges withdur other detectable clinical signs. Complex absence is the term used when other signs are also present.

SEE "WARNINGS" SECTION FOR STATEMENT REGARDING FATAL HEPATIC DYSFUNCTION.

CONTRAINDICATIONS: DEPAROTE (DNALPROEX SODUM) SHOULD NOT BE ADMINISTERED TO PATIENTS WITH HEPATIC DISEASE OR SIGNIFICANT DYSFUNCTION
DEPAROTE E contraindicated in patients with known hypersensitivity to the drug.

CONTRAINDICATIONS: DEPANOTE (ONAL PROEX SODIMIN SHOULD NOT BE ADMINISTERED TO PATENTS WITH HEPATIC DISEASE OR SIGNECANT OVSCILLATION.)

DEPANOTE'S contraindicated in patients with known hypersensitivity to the drug.

WARRINGS: Meastic failure resulting in frastition has occurred in patients receiving valproic acid. These incidents usually account of the patients of the patients and patients are controlled to the patients of th

PRECAUTIONS: Hepatic Dysfunction: See "Based Warning." Contradictions" and "Warnings" sections.

General: Because of reports of thrombocytopenia, whichtion of the secondary phase of platelet aggregation, and abnormal coagulation parameters, platelet counts and coagulation tests are recommended before initiating therapy and a periodic intervals. It is recommended the patients receiving DEPAIDITE (divisipres sodium) be monitored for platelet count and coagulation parameters prior to planned surgery. Evidence of hermotherapy busings or a disorder of hemostack-coagulation as in indication for reduction of DEPAIDITE divisipres and indication of the control of DEPAIDITE divisipres and indications of the control of DEPAIDIT

stapy. Hyperammonemia with or without lethargy or coma has been reported and may be present in the absence of abnormal liver function tests Linically significant elevation occus. DEPAKOTE should be discontinued. Since DEPAKOTE (divalproes sodium) may interact with concurrently administered antiepideptic drugs, perodic serum level determina-ns of concomitant antiepideptic drugs are recommended during the early course of therapy. (See "Drug Interactions" section).

related trend for beingn pulmonary agenomas in male mice receiving varyors acts. It is symma, mice to trace manage to mice is being present.

Mutagenesis: Studies on valproic acid have been performed using bacterial and mammalian systems. These studies have provided previously of mutagenic potential for DEPAKOTE

Fertifity: Chronic toxicity studies in pyrenite and adult rats and dogs demonstrated reduced spermatogenesis and testicular atrophy at doses greater than 200 mg/kg/day in rats and greater than 90 mg/kg/day in dogs. Segment Iterility studies in rats have shown doses up to 350 mg/kg/day for 60 days to have no effect on fertility. THE EFFECT OF DEPAKOTE (DWALPROEX SODIUM) ON THE DEVELOPMENT OF THE TESTES AND ON SPERM PRODUCTION AND FERTIFITY IN HUMANS. SUKKNOWN.

Praganary: Pregnancy Category D: See "Warnings" section.

Mutaging Mothers: Valproate is excerted in heast affice. Concentrations in breast milk have been reported to be 1-10% of serum concentrations. It is not known what effect this would have on a nursing effant. Caution should be exercised when DEPAKOTE is administered to a nursing on woman.

ADVERSE REACTIONS: Since valproir, acid and its derivatives have usually been used with other antiepileptic drugs, it is not possible, in most cases, to determine whether the following adverse reactions can be ascribed to valproic acid alone, or the combination of drugs. Gestrointestimal. The most commonly reported side effects at the ministion of therapy are naises, womining and indigestion. These effects are usually transient and rarely require discontinuation of therapy. Disarrhes, abdominal cramps and constipation have been reported. But an ancessal expertive with weight gain have also been reported. The administration of enterior, costed deviaproses sodium may result in reduction of gestrointestinal side effects in some patients?

ONE Offects: Sodium effects have been noted in patients receiving options acid alone but are found most often in patients receiving combination therapy. Sedation effects have been noted in patients receiving uniformed and may be dose restanted. Assiss, headeder, instiguant, dolloper, asterius, "Spots brider eyer," Sportshiria, dizzess in hard is a New Perior observed of the patients receiving valprois acid alone but are found to the patients receiving the patients of the patients and may be dose restanted. Assiss, headeder, instiguant, dospous, asterius, "Spots brider eyer," Spotshiria, dizzess in hard is only here observed Stan In ash and erythem an unfortioner and hybe been noted. Psychiatric: Emotional layest, depression, psychosis, aggression, hyperactivity and behavioral deterioration have been reported. Musicus/disables."

Demonstration of the Committee of the Co

Other: Edema of the extremities has been reported.

OVERDISAGE. Overlosage with valpois acid may result in deep coma.

Since DEPAKOTE tablets are enteric coated, the benefit of gestric lavage or emesis will vary with the time since ingestion. General supportive measures should be spilled with particular attention bearing given to the maniferenance of adequate uninary output.

Nationarch has been reported to reverse the CNS depressage infects of valproste overdosage. Because nationore could theoretically also reverse the antiepileptic effects of DEPAKOTE is should be used with caution.

reverse the antiepileptic effects of DEPAKOTE a should be used with caution.

DOSAGE_AND_ADMINISTRATION_OF DEPAKOTE is administed or only. The recommended initial dose is 15 mg/kg/day, increasing at one verse intervals by 5 to 10 mg/kg/day with secures are controlled or side effects precided further necessor. The maximum recommend-efficacy is 10 mg/kg/day. If the includ alsh dose exceeds C25 mg is should be given as disorded regimeneases. The maximum recommend-efficacy is 10 mg/kg/day. If the includ alsh dose exceeds C25 mg is should be given as disorded therapy. DEPAKOTE should be initiated at the same total daily dose and disoing schedule. After the patient is stated on DEPAKOTE, a vivice a day or three times a day schedule may be instituted in selected patients. The frequency of adverse efficis (staticularly elevated liver enzymes) may be dose related. The benefit of improved secius consolivation was accompany higher doses should therefore be weighed against the possibility of a greater incidence of adverse maximum. A good correlation has not been established between daily dose, secure nevel and the appoint effect. However, therapeutic valprouse serum levels for most patients will range from 50 to 100 mcg/ml. Occasional patients may be controlled with serum levels fower or higher than this range.

serum levels for most patients will range from 50 to 100 ms/mil. Occasions produced than his range.

As the DEPAKOTE dosage is titrated upward, blood levels of phenobarbital and/or phenytoin may be affected. (See "Precautions" secny. Patients who experience G. I. irritation may benefit from administration of the drug with food or by slowly building up the dose from an ini-

HOW SUPPLIED: DEPAKOTE (divalorner sodium enteric coated tablets) are supplied as

125 mg salmon pink-colored tablets:	
Bottles of 100	(MDC 0074-6212-13)
250 mg peach-colored tablets:	
Bottles of 100	(NDC 0074-6214-13)
Abbo-Pac® unit dose packages of 100	(NDC 0074-6214-11)
500 mg lavender-colored tablets:	
Bottles of 100	(NDC 0074-6215-13)
Abbo Pac® unit dose packages of 100	(NDC 0074-6215-11)

PROOF Fa. Unit was penages.

REFERENCES

Centers for Disease Control, Valproate: A New Cause of Birth Defects — Report from Italy and Follow up from France, Marbidity and Mortally Week/Rapport 22(23)1.438-439, August 26, 1983.

Wilder, B.J. et al. Gastrointestnal Tolerance of Divalgroes Sodium. Neurology 33,808-811, June, 1983.

Wilder, B.J. et al. Twice-Daily Dosing of Valgroate with Divalgroes. Clin Pharmacol Ther 34(4): 501-504, 1983.

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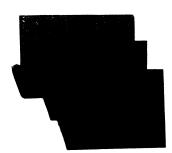
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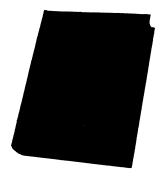


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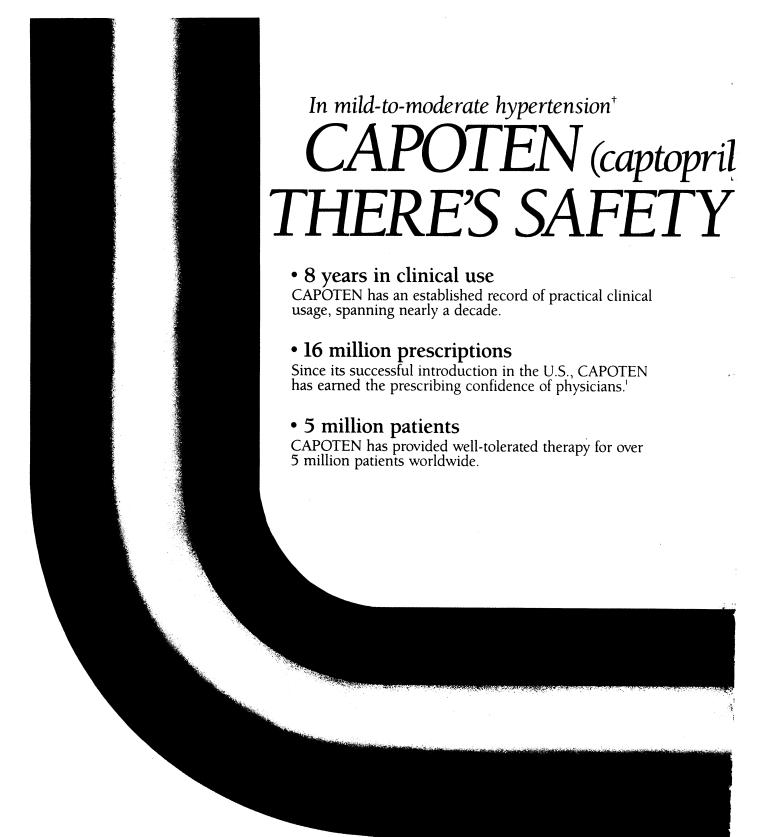
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†CAPOTEN may be used as initial therapy only for patients with normal renal function in whom the risk of neutropenia/ agranulocytosis is relatively low (1 out of over 8,600 in clinical trials). Use special precautions in patients with impaired renal function, collagen vascular disorders, or those exposed to other drugs known to affect the white cells or immune response. Evaluation of hypertensives should always include assessment of renal function. See INDICATIONS AND USAGE, WARNINGS, and ADVERSE REACTIONS in the brief summary on the adjacent page.



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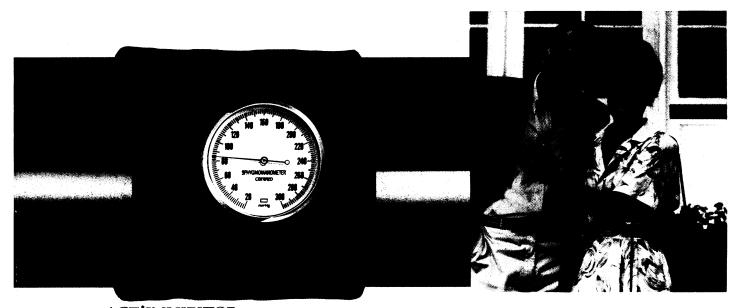
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Comparison of Adverse Effects for CAPOTEN (\leq 100 mg) versus Placebo in Hypertensive Patients with Normal Renal Function (N = 1,622)‡ 1

71		
ADVERSE EFFECT	CAPOTEN (N = 1,174) (% affected)	Placebo (N = 448) (% affected)
Headache	5.2	6.9
Rash	3.7	2.5
Dizziness	3.5	2.0
Nausea	3.2	2.0
Fatigue	3.1	2.0
Taste alteration	1.5	1.1
Gastrointestinal	1.4	0.7
Diarrhea	1.1	1.1

*None of the differences between captopril and placebo was statistically significant. For the most part, adverse effects were mild and transient and usually did not require discontinuation of therapy. Only 5.5% of the patients in this data base discontinued because of an adverse effect. Data include adverse effects for CAPOTEN with an incidence greater than 1%.



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CAPOTEN® TABLETS Captopril Tablets

INDICATIONS: Hypertension — CAPOTEN (captopril) is indicated for the treatment of hypertension. Consideration should be given to the risk of neutropenia/agranulocytosis (see WARNINGS). CAPOTEN may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for those who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations. CAPOTEN is effective alone and in combination with other antihypertensive agents, especially thiazide-type diuretics.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

WARNINGS: Neutropenia/Agranulocytosis — Neutropenia (<1000/mm³) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

In clinical trials in patients with hypertension who have normal renal function (serum creatinine $<1.6\ mg/dL$ and no collagen vascular disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) but no collagen vascular disease, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus erythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during subsequent clinical experience. Of reported cases, about half had serum creatinine $\geq 1.6\ mg/dL$ and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present.

Neutropenia has appeared usually within 3 months after starting therapy, associated with myeloid hypoplasia and frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophils generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors.

Evaluation of the hypertensive or heart failure patient should always include assessment of renal function. If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, fever); if infection is suspected, perform counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count < 1000/mm³) withdraw captopril and closely follow the patient's course.

Proteinuria — Total urinary proteins >1 g/day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (>150 mg/day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy, patients with prior renal disease or those receiving captopril at doses >150 mg/day should have urinary protein estimates (dip-stick on 1st morning urine) before therapy, and periodically thereafter.

Hypotension – Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]).

In heart failure, where blood pressure was either normal or low, transient decreases in mean blood pressure >20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: Impaired Renal Function, Hypertension—Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure—About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. Valvular Stenosis—A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis due to decreased afterload reduction.

 ${\it Surgery/Anesthesia-If hypotension occurs during major surgery or an esthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.}$

Drug Interactions: Hypotension: Patients on Diwretic Therapy — Precipitous reduction of blood pressure may occasionally occur within the 1st hour after administration of the initial captopril dose in patients on diuretics, especially those recently placed diuretics, and those on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy or by initiating therapy with small doses (6.25 or 12.5 mg). Alternatively, provide medical supervision for at least 1 hour after the initial dose.

 $\label{eq:Agents} \textit{Agents Having Vasodilator Activity} - \text{In heart failure patients, vasodilators should} \\ \text{be administered with caution.}$

Agents Causing Renin Release — Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity — The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium — Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Use potassium-containing salt substitutes with caution.

Inhibitors of Endogenous Prostaglandin Synthesis — Indomethacin and other nonsteroidal anti-inflammatory agents may reduce the antihypertensive effect of captopril, especially in low renin hypertension.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acctone

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Pregnancy: Category C – There are no adequate and well-controlled studies in pregnant women. Embryocidal effects and craniofacial malformations were observed in rabbits. Therefore, captopril should be used during pregnancy, or for patients likely to become pregnant, only if the potential benefit outweighs the potential risk to the fetus. Captopril crosses the human placenta.

Nursing Mothers: Captopril is secreted in human milk. Exercise caution when administering captopril to a nursing woman, and, in general, nursing should be interrupted.

Pediatric Use: Safety and effectiveness in children have not been established although there is limited experience with use of captopril in children from 2 months to 15 years of age. Dosage, on a weight basis, was comparable to that used in adults. Captopril should be used in children only if other measures for controlling blood pressure have not been effective.

ADVERSE REACTIONS: Reported incidences are based on clinical trials involving approximately 7000 patients.

Renal — About 1 of 100 patients developed proteinuria (see WARNINGS). Renal insufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1000 patients.

Hematologic - Neutropenia/agranulocytosis have occurred (see WARNINGS). Anemia, thrombocytopenia, and pancytopenia have been reported.

Dermatologic — Rash (usually maculopapular, rarely urticarial), often with pruritus and sometimes with fever and eosinophilia, in about 4 to 7 of 100 patients (depending on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, without rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, and photosensitivity have also been reported. Angioedema of the face, mucous membranes of the mouth, or of the extremities in about 1 of 1000 patients — reversible on discontinuance of captopril therapy. One case of laryngeal edema reported. Flushing or pallor in 2 to 5 of 1000 patients.

Cardiovascular — Hypotension may occur, see WARNINGS and PRECAUTIONS (Drug Interactions) for discussion of hypotension on initiation of captopril therapy. Tachycardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pectoris, myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 2 to 3 of 1000 patients.

Dysgeusia – About 2 to 4 (depending on renal status and dose) of 100 patients developed a diminution or loss of taste perception; taste impairment is reversible and usually self-limited even with continued drug use (2 to 3 months). Gastric irritation, abdominal pain, nausea, vomiting, diarrhea, anorexia, constipation, aphthous ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, dyspnea, cough, alopecia, and paresthesias reported in about 0.5 to 2% of patients but did not appear at increased frequency compared to placebo or other treatments used in controlled trials.

Altered Laboratory Findings: Elevations of liver enzymes in a few patients although no causal relationship has been established. Rarely cholestatic jaundice and hepatocellular injury with or without secondary cholestasis, have been reported. A transient elevation of BUN and serum creatinine may occur, especially in volume-depleted or renovascular hypertensive patients. In instances of rapid reduction of longstanding or severely elevated blood pressure, the glomerular filtration rate may decrease transiently, also resulting in transient rises in serum creatinine and BUN. Small increases in serum potassium concentration frequently occur, especially in patients with renal impairment (see PRECAUTIONS).

OVERDOSAGE: Primary concern is correction of hypotension. Volume expansion with an I.V. infusion of normal saline is the treatment of choice for restoration of blood pressure. Captopril may be removed from the general circulation by hemodialysis.

DOSAGE AND ADMINISTRATION: CAPOTEN (captopril) should be taken one hour before meals. In hypertension, CAPOTEN may be dosed bid or tid. Dosage must be individualized; see DOSAGE AND ADMINISTRATION section of package insert for detailed information regarding dosage in hypertension and in heart failure. Because CAPOTEN (captopril) is excreted primarily by the kidneys, dosage adjustments are recommended for patients with impaired renal function.

Consult package insert before prescribing CAPOTEN (captopril).

HOW SUPPLIED: Available in tablets of 12.5, 25, 50, and 100 mg in bottles of 100 (25 mg also available in bottles of 1000), and in UNIMATIC* single dose packs of 100 tablets. (J3-658D)

Reterences

- 1. PDS Alpha, National Prescription Report, Pharmaceutical Data Services, Subsidiary of McKesson Corporation.
- 2. Data on file, Squibb Institute for Medical Research.



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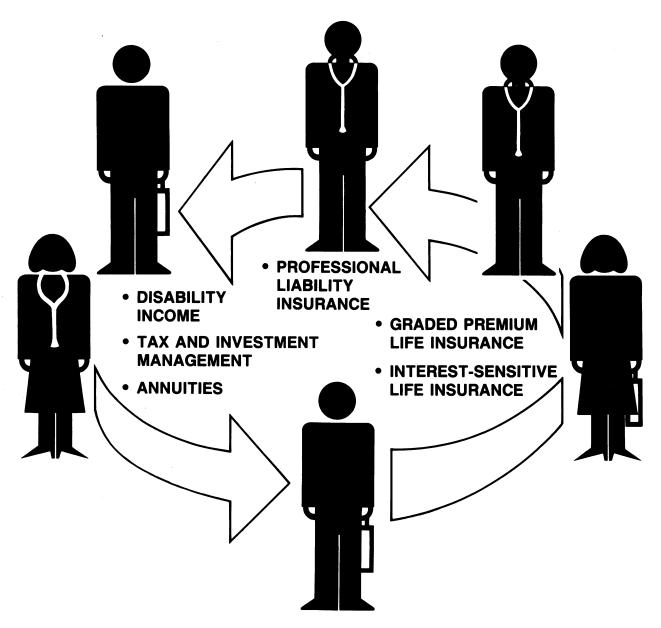
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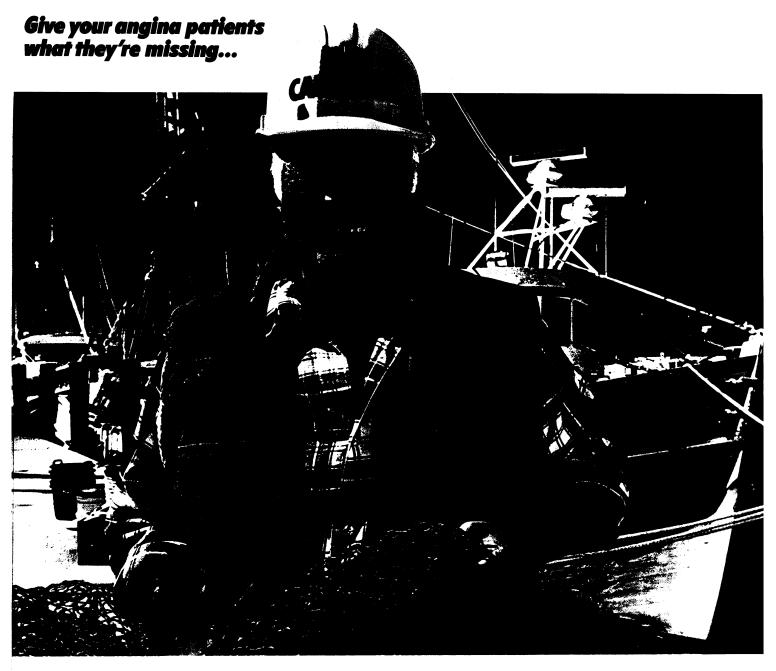
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CARDIZEM: FEW SIDE EFFECTS

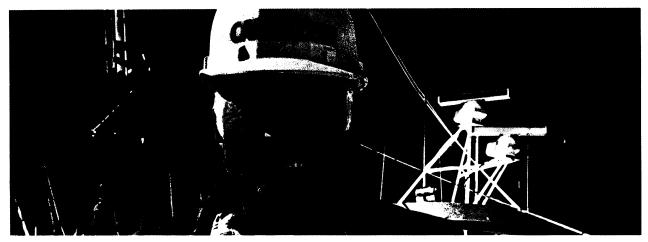
diltiazem HCI/Marion



- Antianginal action includes dilatation of coronary arteries, a decrease in vascular resistance/afterload, and a reduction in heart rate
- Proven efficacy when used alone in angina'
- Compatible with other antianginals 2,3*
- A safe choice for angina patients with coexisting hypertension, asthma, COPD, or PVD^{4,5}

*See Warnings and Precautions.

Please see brief summary of prescribing information on the next page.



FEW SIDE EFFECTS IN ANTIANGINAL THERAPY diltiazem HCI/Marion

60 mg tid or qid

Brief Summary Professional Use Information

(diltiazem HCl) 30 mg and 60 mg Tablets

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacernaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic). WARNINGS

- Cardiac Conduction. CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result sick sinus synutorie. This effect intoy rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of distult in addition beta blocking or distribution and distult in addition. beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of
- Congestive Heart Failure. Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using
- the drug in such patients.

 Hypotension. Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.

 Acute Hepatic Injury. In rare instances, significant selectricing
- elevations in enzymes such as alkaline phospha-tase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been on sistem with outer repaire injuly i have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but propable in some. (See PRECAUTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bite. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of dittiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 ma/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these

changes were reversible with continued dosing. **Drug Interaction.** Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diffiazem has been shown to increase count discussion length us to 2009.

serum digoxin levels up to 20%. Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bácterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater. There are no well-controlled studies in pregnant

women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that

patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded. In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placeboo therapy. The following represent accurrences observed in

The following represent occurrences observed in clinical studies which can be at least reasonably asso-

ciated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%). Cardiovascular:

Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpi-

tations, syncope.

Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.

Gastrointestinal-Anorexia, constipation, diarrhea,

dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight

increase.

Nervous System:

Dermatologic. Petechiae, pruritus, photosensitivity,

urticaria.

Other: Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasai congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties

The following postmarketing events have been reported infrequently in potients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be applicabilities. Issued 7/86

See complete Professional Use Information before prescribina.

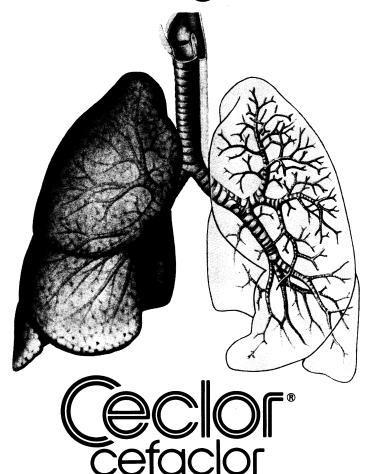
References: 1. Pepine CJ, Feldman RL, Hill JA, et al: Clinical outcome after treatment of rest angina with Clinical outcome arier treatment of rest angina with calcium blockers: Comparative experience during the initial year of therapy with diffiazem, nifedipine, and verapamil. Am Heart J. 1983; 106(6):1341-1347.

2. Shapiro W: Calcium channel blockers: Actions on the heart and uses in ischemic heart disease. Consultant 1984;24(Dec):150-159.

3. Johnston DL, Lesoway R, Humen DP, et al: Clinical and hemodynamic evaluation of propranolol in combination with verapamil, nifedipine and diltiazem in exertional angina pectoris: A placebo-controlled, double-blind, randomized, crossover study. Cominied, adulation in Michael (1985) 15-680-687. 4. Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39. 5. Schroeder JS: Calcium and bela blockers in ischemic heart disease: When to use which. Mod Med 1982-65(Sept.) (4.116) 1982;50(Sept):94-116



Consider the causative organisms...



250-mg Pulvules[®] t.i.d. offers effectiveness against the major causes of bacterial bronchitis

Haemophilus influenzae, Streptococcus pneumoniae (ampicillin-susceptible and ampicillin-resistant)

Note: Ceclor is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Ceclor® (cefactor)

Summary. Consult the package literature for prescribing information.

Indications: Lower respiratory infections, including pneumonia, caused by susceptible strains of Streptococcus pneumoniae, Haemophilus influenzae, and Streptococcus pyogenes (group A β-hemolytic streptococci)

Contraindication:

Known allergy to cephalosporins

Warnings:

CECLOR SHOULD BE ADMINISTERED CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. PENICILLINS AND CEPHA-LOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY. POSSI-BLE REACTIONS INCLUDE ANAPHYLAXIS.

Administer cautiously to allergic patients. Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of
- nonsusceptible organisms.

 Positive direct Coombs' tests have been re-
- ported during treatment with cephalosporins.

 Ceclor should be administered with caution in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be pre-scribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients) Therapy-related adverse reactions are uncommon. Those reported include:

prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Penicillin is the usual drug of choice in the treatment and

- Gastrointestinal (mostly diarrhea): 2.5%
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treat-
- · Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, and serum-sickness-like reactions that have included erythema multiforme [rarely, Stevens-Johnson syndrome] or the above skin manifestations accompanied by arthritis/ arthralgia and, frequently, fever): 1.5%; usually subside within a few days after cessation of therapy. Serum-sickness-like reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Cector. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a his-
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness,

insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.

Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%; and, rarely, thrombocytopenia.

Abnormalities in laboratory results of uncertain etiology

- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children).
- Abnormal urinalysis; elevations in BUN or serum creatinine.
- · Positive direct Coombs' test.
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly). [072886R]

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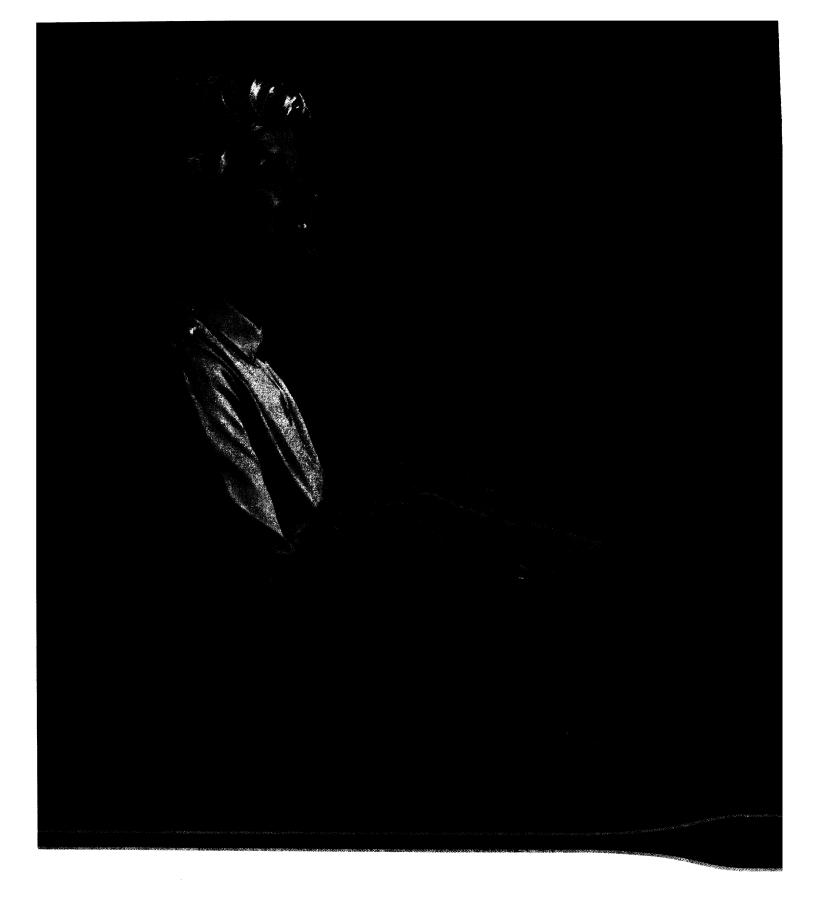
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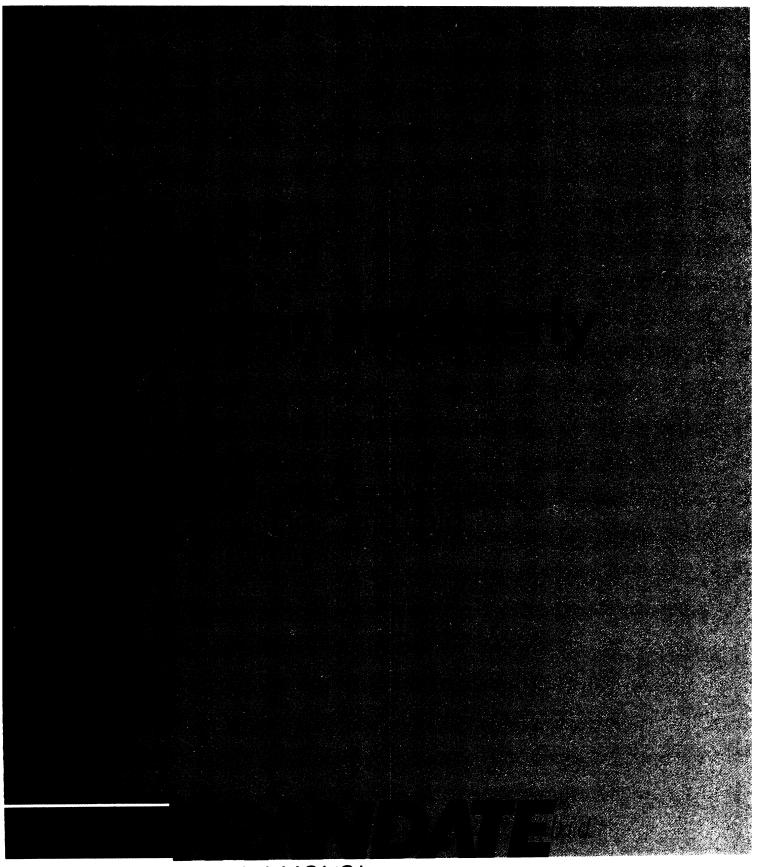


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Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285.

Eli Lilly Industries, Inc Carolina, Puerto Rico 00630





labetalol HCI/Glax0 100 mg/200 mg tablets
Because it also
vasodilates

References: 1. Holtzman JL, Finley D, Johnson B, et al: The effects of single-dose atenolol, labetalol, and propranolol on cardiac and vascular function. Clin Pharmacol Ther 1986;40:268-273. 2. Due DL, Giguere GC, Plachetka JR: Postmarketing comparison of labetalol and propranolol in hypertensive patients. Clin Ther 1986;8(6):624-631. 3. Burris JF, Goldstein J, Zager PG, et al: Comparative tolerability of labetalol versus propranolol, atenolol, pindolol, metoprolol, and nadolol. J Clin Hypertens 1986;3:1-9. 4. Eth RJ, Plachetka JR: Thermographic evaluation of the peripheral vascular effects of labetalol and propranolol. Curr Ther Res 1985;28(1):68-73.

TRANDATE® Tablets (labetalol hydrochloride)

BRIEF SUMMARY OF PRODUCT INFORMATION

The following is a brief summary only. Before prescribing, see complete prescribing information in TRANDATE® Tablets product labeling.

HIDICATIONS AND USAGE: TRANDATE® Tablets are indicated in the management of hypertension.

TRANDATE Tablets may be used alone or in combination with other antihypertensive agents, especially thiazide and loop diuretics.

CONTRAINDICATIONS: TRANDATE® Tablets are contraindicated in bronchial asthma, overt cardiac failure

CONTRAINDICATIONS: TRANDATE® Tablets are contraindicated in bronchial asthma, overt cardiac failure, greater-than-first-degree heart block, cardiogenic shock, and severe bradycardia (see WARNINGS). WARNINGS: Cardiac Failures: Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure. Beta-blockade carries a potential hazard of further depressing myocardial contractility and precipitating more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary labetalol HCl can be used with caution in patients with a history of heart failure wha are well compensated. Congestive heart failure has been observed in patients receiving labetalol HCl. Labetalol HCl does not abolish the inotropic action of digitalis on heart muscle.

In Patients Without a History of Cardiac Failure: In patients with latent cardiac insufficiency, continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of impending cardiac failure, patients should be high digitalized and/or be given a diuretic, and the response should be observed closely. If cardiac failure continues despite adequate digitalization and diuretic, TRANDATE® therapy should be withdrawn (gradually, if possible).

possiner,

Exacerbation of Ischemic Heart Disease Following Abrupt Withdrawal: Angina pectoris has not been reported upon labetalol HCI discontinuation. However, hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after abrupt discontinuation of such therapy. When discontinuing myocardial infarction have occurred after abrupt discontinuation of such therapy. When discontinuing chronically administered TRANDATE, particularly in patients with ischemic heart disease, the dosage should be gradually reduced over a period of one to two weeks and the patient should be carefully monitored. If angina markedly worsens or acute coronary insufficiency develops, TRANDATE administration should be reinstituted promptly, at least temporarily, and other measures appropriate for the management of unstable angina should be taken. Patients should be warned against interruption or discontinuation of therapy without the physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue TRANDATE therapy abruptly even in patients treated only for hyportension.

types cleasure.

Monallergic Bronchospasm (eg. Chronic Bronchitis and Emphysema): Patients with bronchospastic disease should, in general, not receive beta-blockers. TRANDATE may be used with caution, however patients who do not respond to, or cannot tolerate, other antihypertensive agents. It is prudent, if TRANDATE is used, to use the smallest effective dose, so that inhibition of endogenous or exogenous beta-agonists is minimized

beta-agonists is minimized.

Pheochromocytoma: Labetalol HCl has been shown to be effective in lowering blood pressure and relieving symptoms in patients with pheochromocytoma. However, paradoxical hypertensive responses have been reported in a few patients with this tumor; therefore, use caution when administering labetalol HCl to patients with pheochromocytoma.

Biabets Welditus and Hypogyteemia: Beta-adrenergic blockade may prevent the appearance of premonitory signs and symptoms (eg. tachycardia) of acute hypoglycemia. This is especially important with labile diabetics. Beta-blockade also reduces the release of insulin in response to hyperglycemia; it may there-

Major Surgery: The necessity or desirability of withdrawing beta-blocking therapy prior to major surgery is controversial. Protracted severe hypotension and difficulty in restarting or maintaining a heartbeat have been reported with beta-blockers. The effect of labetalol HCIS alpha-adrenergic activity has not

been evaluated in this setting.

A synergism between labetalol HCl and halothane anesthesia has been shown (see **Brug Interactio** under PRECAUTIONS)

ARECANTIONS: General: Impaired Hepatic Function: TRANDATE® Tablets should be used with caution in patients with impaired hepatic function since metabolism of the drug may be diminished.

Jaundice or Hepatic Dysfunction: On rare occasions, labetalol HCl has been associated with jaundice

(both hepatic and cholestatic). It is therefore recommended that treatment with labetalol HCI be stopped immediately should a patient develop jaundice or laboratory evidence of liver injury. Both have been shown to be reversible on stopping therapy.

Information for Patients: As with all drugs with beta-blocking activity, certain advice to patients being treated with labetalol HCL is warranted. This information is intended to aid in the safe and effective use

treated with labetation it is warranted. This minimation is memored to all in the sale and effective use of this medication. It is not a disclosure of all possible adverse or intended effects. While no incidence of the abrupt withdrawal phenomenon (exacerbation of angina pectoris) has been reported with labetalol HCI, dosing with TRANDATE Tablets should not be interrupted or discontinued without a physician's advice. Patients being treated with TRANDATE Tablets should consult a physician at any sign of impending cardiac failure. Also, transient scalp tingling may occur, usually when treatment with TRANDATE Tablets is initiated (or an MYEDE PRAFTIME). is initiated (see ADVERSE REACTIONS).

is initiated (see ANVENSE REACTIONS).

Laboratory Tests: As with any new drug given over prolonged periods, laboratory parameters should be observed over regular intervals. In patients with concomitant illnesses, such as impaired renal function, appropriate tests should be done to monitor these conditions.

Drug Interactions: In one survey, 2.3% of patients taking labetalol HCl in combination with tricyclic antidepressants experienced tremor as compared to 0.7% reported to occur with labetalol HCl alone. The contribution of each of the treatments to this adverse reaction is unknown, but the possibility of a drug interaction cannot be excluded.

Drugs necession beta, blocking properties can blust the broschedilator offset of beta repeater appoints.

interaction cannot be excluded.

Drugs possessing beta-blocking properties can blunt the bronchodilator effect of beta-receptor agonist drugs in patients with bronchospasm; therefore, doses greater than the normal antiasthmatic dose of beta-agonist bronchodilator drugs may be required.

Cimetidine has been shown to increase the bioavailability of labetalol HCI. Since this could be explained either by enhanced absorption or by an afteration of hepatic metabolism of labetalol HCI, special care should be used in establishing the dose required for blood pressure control in such patients.

Synergism has been shown between halothane anesthesia and intravenously administered labetalol HCI. During controlled hypotensive anesthesia using labetalol HCI in association with halothane, high concentrations (3% or above) of halothane should not be used because the degree of hypotension will be increased and because of the possibility of a large reduction in cardiac output and an increase in central venous pressure. The anesthesiologist should be informed when a patient is receiving labetalol HCI. Labetalol HCI is used with nitroglycerin in patients with angina pectoris, additional antihypertensive effects if abstalol HCI is used with nitroglycerin in patients with angina pectoris, additional antihypertensive effects may occur.

tensive effects may occur.

tensive effects may occur.

Drug/Laboratory Test Interactions: The presence of a metabolite of labetalol in the urine may result in falsely increased levels of urinary catecholamines when measured by a nonspecific trihydroxyindole (THI) reaction. In screening patients suspected of having a pheochromocytoma and being treated with labetalol HCI, specific radioenzymatic or high performance liquid chromatography assay techniques should be used to determine levels of catecholamines or their metabolites.

Carcinogenesis, Mutagenesis, impairment of Fertility: Long-term oral dosing studies with labetalol HCI for 18 months in mice and for two years in rats showed no evidence of carcinogenesis. Studies with labetalol HCI using dominant lethal assays in rats and mice and exposing microorganisms according to modified hear tests between an evidence of mutagenesis.

modified Ames tests showed no evidence of mutagenesis.

Pregnancy: Teratogenic Effects: Pregnancy Category C: Teratogenic studies have been performed with

TRAMBATE® Tablets (labetalol hydrochloride)

labetalol in rats and rabbits at oral doses up to approximately six and four times the maximum recommended human dose (MRHD), respectively. No reproducible evidence of fetal malformations was observed. Increased fetal resorptions were seen in both species at doses approximating the MRHD. There are no adequate and well-controlled studies in pregnant women. Labetalol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Montaratogenic Effects: Infants of mothers who were treated with labetalol HCl during pregnancy did not appear to be adversely affected by the drug. Oral administration of labetalol to rats during late gestation through weaning at doses of two to four times the MRHD caused a decrease in neonatal survival.

**Labor and Delivery: Labetalol HCl given to pregnant women with hypertension did not appear to affect the usual course of labor and delivery.

**Wursing Mothers: Small amounts of labetalol (approximately 0.004% of the maternal dose) are excreted in human milk. Caution should be exercised when TRANDATE Tablets are administered to a nursing woman.

**Podlatric Usa: Safety and effectiveness in children have not been established.

**ADVERSE ERACTIONS: Nots adverse effects are mild, transient, and occur early in the course of treatment. In controlled clinical trials of three to four months' duration, discontinuation of TRANDATE® Tablets due to one or more adverse effects was required in 7% of all patients. In these same trials, beta-blocker control agents led to discontinuation in 8% to 10% of patients, and a centrally acting alpha-agonist in 30% of patients.

The following adverse reactions were derived from multi-center, controlled clinical trials over treatment The following adverse reactions were derived from multi-center, controlled clinical trials over treatment periods of three and four months. The rates, which ranged from less than 1% to 5% except as otherwise noted, are based on adverse reactions considered probably drug-related by the investigator (if all reports are considered, the rates are somewhat higher (eg, dizziness, 20%; nausea, 14%; fatigue, 11%). Body as a Whole: Fatigue, asthenia, and headache.

Gastrointestinal: Nausea (6%), wmiting, dyspepsia, diarrhea, and taste distortion.

Central and Paripheral Nervous Systems: Dizziness (11%), paresthesia, and drowsiness.

Autonomic Nervous System: Nasal stuffiness, ejaculation failure, impotence, and increased

Cardiovascular: Edema and postural hypotension.

Respiratory: Dyspnea.

Skin: Rash

Special Senses: Vision abnormality and vertigo.

The adverse effects were reported spontaneously and are representative of the incidence of adverse effects that may be observed in a properly selected hypertensive patient population, ie, a group excluding patients with bronchospastic disease, overt congestive heart failure, or other contraindications to beta-

Clinical trials also included studies utilizing daily doses up to 2,400 mg in more severely hypertensive patients. The US therapeutic trials data base for adverse reactions that are clearly or possibly dose-related shows that the following side effects increased with increasing dose: dizziness, fatigue, nausea, vomiting, dyspepsia, paresthesia, nasal stuffiness, ejaculation failure, impotence, and edema.

In addition, a number of other less common adverse events have been reported in clinical trials or the

Cardiovascular: Postural hypotension, including rarely, syncope.

Cantral and Paripharal Nervous Systems: Paresthesias, most frequently described as scalp tingling.
most cases, it was mild, transient, and usually occurred at the beginning of treatment.

Collagen Disorders: Systemic lupus erythematosus; positive antinuclear factor (ANF).

Eyes: Dry eyes.

Immunological System: Antimitochondrial antibodies.

Liver and Biliary System: Cholestasis with or without jaundice.

Musculoskeletal System: Muscle cramps; toxic myopathy.

Respiratory System: Bronchospasm.

Skin and Appendages: Rashes of various types, such as generalized maculopapular, lichenoid, urticarial, bullous lichen planus, psoriaform, and facial erythema; Peyronie's disease; reversible alopecia.

Urinary System: Difficulty in micturition, including acute urinary bladder retention.

Ellowing approach for marketing in the United Microdom amounted release user insubing approach.

Following approval for marketing in the United Kingdom, a monitored release survey involving approximately 6,800 patients was conducted for further safety and efficacy evaluation of this product. Results of this survey indicate that the type, severity, and incidence of adverse effects were comparable to those

Potential Adverse Effects: In addition, other adverse effects not listed above have been reported with

Other beta-adrenergic blocking agents.

Central Nervous System: Reversible mental depression progressing to catatonia, an acute reversible Contral Networks System: Reversible mental depression progressing to catatonia, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance or neuropsychometrics.

Cardiovascular: Intensification of AV block (see CONTRAINDICATIONS).

Allargic: Fever combined with aching and sore throat; laryngospasm; respiratory distress.

Hematologic: Agranulocytosis; thrombocytopenic or nonthrombocytopenic purpura.

Gastrointestinal: Mesenteric artery thrombosis; ischemic colitis.

The oculomucocutaneous syndrome associated with the beta-blocker practolol has not been reported

Clinical Laboratory Tests: There have been reversible increases of serum transaminases in 4% of patients treated with labetalol HCl and tested, and more rarely, reversible increases in blood urea.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescrib-

ng information. **Dosage and administration**: Dosage must be individualized. The recommended *initial* dosage is 100 mg twice daily whether used alone or added to a diuretic regimen. After two or three days, using standing blood pressure as an indicator, dosage may be titrated in increments of 100 mg bid every two or

standing blood pressure as an indicator, dosage may be titrated in increments of 100 mg bid every two or three days. The usual maintenance dosage of labetalol HCl is between 200 and 400 mg twice daily. Before use, see complete prescribing information for dosage details.

HOW SUPPLIED: TRANDATE 100 GLAXO; bottles of 100 (NDC 0173-0346-43) and 500 (NDC 0173-0346-44) and unit dose packs of 100 tablets (NDC 0173-0346-47).

TRANDATE Tablets, 200 mg, white, round, scored, film-coated tablets engraved on one side with "TRANDATE Tablets, 200 mg, white, round, scored, film-coated tablets engraved on one side with "TRANDATE Tablets, 300 mg, peach, round, scored, film-coated tablets engraved on one side with "TRANDATE Tablets, 300 mg, peach, round, scored, film-coated tablets engraved on one side with "TRANDATE Tablets, 300 GLAXO;" bottles of 100 (NDC 0173-0347-43) and 500 (NDC 0173-0348-44) and unit dose packs of 100 tablets (NDC 0173-0348-47).

TRANDATE Tablets should be stored between 2° and 30°C (36° and 86°F). TRANDATE Tablets in the unit dose boxes should be protected from excessive moisture.

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September 1986



The portrait of anxiety

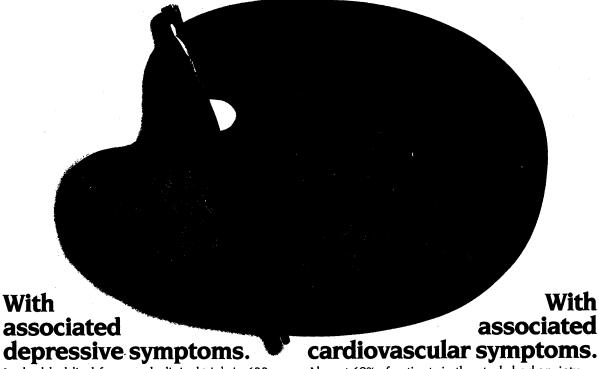


UpjohnThe Upjohn Company
Kalamazoo Michigan 49001 USA

Please see adjacent page for brief summary of prescribing information.

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is often complicated



In double-blind, four-week clinical trials in 632 patients with moderate to severe anxiety, therapy with XANAX was compared with placebo.

XANAX was significantly more effective (P<001) than placebo in relieving the anxiety with over half of the patients showing marked to moderate improvement by the first evaluation period (one week).

In addition, over 70% of these patients

experienced associated moderate to severe depressed mood. XANAX was shown to be signifi-cantly more effective (P<.014) than placebo in improving the associated depressed mood.



Almost 60% of patients in the study had anxiety with associated cardiovascular symptoms even though cardiovascular disease had been ruled out. XANAX was shown to effectively relieve anxiety including the associated cardiovascular symptoms.

XAŇAX, the first of a unique class—the

triazolobenzodiazepines.

■ Well tolerated—Side effects, if they occur, are generally observed at the beginning of therapy and usually disappear with continued medica-

tion. Drowsiness and light-headedness were the most commonly reported adverse reactions.

Sustained efficacy—No reported increase in dosage during 16-week clinical study, once an appropriate dosage was achieved. Since long-term effectiveness of XANAX has not been established, it is recommended that it not be used for longer than 16 weeks.

■ Simple dosage—0.25 to 0.5 mg ti.d.



for the relief of complicated anxiety

XANAX* Tablets (alprazolam) @

CONTRAINDICATIONS

Patients with sensitivity to this drug or other benzodiazepines and in acute narrow angle glaucoma.

WARNINGS

Not of value in psychotic patients. Caution patients against hazardous occupations requiring complete mental alertness and about the simultaneous ingestion of alcohol and other CNS depressant drugs.

Benzodiazepines can cause fetal harm in pregnant women. Warn patients of the potential hazard to the fetus. Avoid during the first trimester.

PRECAUTIONS

General: The dosage of XANAX Tablets should be reduced or withdrawn gradually, since withdrawal seizures have been reported upon abrupt withdrawal. If XANAX is combined with other psychotropics or anticonvulsant drugs, consider drug potentiation (see Drug Interaction section). Exercise the usual precautions regarding size of the prescription for depressed or suicidal patients. In elderly and debilitated patients, use the lowest possible dosage (see Dosage and Administration). Observe the usual precautions in treating patients with impaired renal or hepatic function.

Information for Patients: Alert patients about: (a) consumption of alcohol and drugs, (b) possible fetal abnormalities, (c) operating machinery or driving, (d) not increasing dose of the drug due to risk of dependence, (e) not stopping the drug abruptly. Laboratory Tests: Not ordinarily required in otherwise healthy patients. Drug Interactions: Additive CNS depressant effects with other psychotropics, anticonvulsants, antihistamines, ethanol and other CNS depressants. Pharmacokinetic interactions with other drugs, e.g., cimetidine, have been reported. Drug/Laboratory Test Interactions: No consistent pattern for a drug or test. Carcinogenesis, Mutagenesis, Impairment of Fertility: No carcinogenic potential or impairment of fertility in rats. Pregnancy: See Warnings. Nonleratogenic Effects: The child born of a mother on benzodiazepines may be at some risk for withdrawal symptoms and neonatal flaccidity. Labor and Delivery: No established use. Nursing Mothers: Benzodiazepines are excreted in human milk. Women on XANAX should not nurse. Pediatric Use: Safety and effectiveness in children below the age of 18 have not been established.

ADVERSE REACTIONS

Side effects are generally observed at the beginning of therapy and usually disappear with continued medication. In the usual patient, the most frequent side effects are likely to be an extension of the pharmacologic activity of XANAX, e.g., drowsiness or lightheadedness.

Central nervous system: Drowsiness, lightheadedness, depression, headache, confusion, insomnia, nervousness, syncope, dizziness, akathisia, and tiredness/ sleepiness. Castrointestinal: Dry mouth, constipation, diarrhea, nausea/vomiting, and increased salivation. Cardiovascular: Tachycardia/palpitations, and hypotension. Sensory: Blurred vision. Musculoskeletal: Rigidity and tremor. Cutaneous: Dermatitis/allergy. Other side effects: Nasal congestion, weight gain, and weight loss. Withdrawal seizures have been reported upon rapid decrease or abrupt discontinuation of XANAX. (See Precautions.)

In addition, the following adverse events have been reported with the use of benzodiazepines: dystonia, irritability, concentration difficulties, anorexia, transient amnesia or memory impairment, loss of coordination, fatigue, sedation, slurred speech, jaundice, musculoskeletal weakness, pruritus, diplopia, dysarthria, changes in libido, menstrual irregularities, incontinence and urinary retention.

Paradoxical reactions such as stimulation, agitation, increased muscle spasticity, sleep disturbances, and hallucinations may occur. Should these occur, discontinue the drug.

During prolonged treatment, periodic blood counts, urinalysis, and blood chemistry analysis are advisable. Minor EEG changes, of unknown significance, have been observed.

DRUG ABUSE AND DEPENDENCE

Physical and Psychological Dependence: Withdrawal symptoms have occurred following abrupt discontinuance of benzodiazepines. Withdrawal seizures have occurred upon rapid decrease or abrupt discontinuation of therapy. In all patients, dosage should be gradually tapered under close supervision. Patients with a history of seizures or epilepsy should not be abruptly withdrawn from XANAX. Addiction-prone individuals should be under careful surveillance. Controlled Substance Class: XANAX is a controlled substance and has been assigned to schedule IV.

OVERDOSAGE

Manifestations include somnolence, confusion, impaired coordination, diminished reflexes and coma. No delayed reactions have been reported.

DOSAGE AND ADMINISTRATION

Dosage should be individualized.

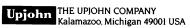
The usual starting dose is 0.25 to 0.5 mg, t.i.d. Maximum total daily dose is 4 mg. In the elderly or debilitated, the usual starting dose is 0.25 mg, two or three times daily. Reduce dosage gradually when terminating therapy, by no more than 0.5 milligram every three days.

HOW SUPPLIED

XANAX Tablets are available as 0.25 mg, 0.5 mg, and 1 mg tablets.

Caution: Federal law prohibits dispensing without prescription.

B-5-S

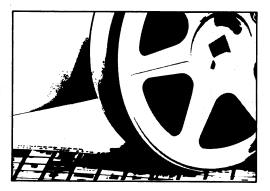


J-7384 February 1987



A GREAT WAY TO SERVE

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State	Zip.	

24-hour security for the hypertensive heart

First-step cardiovascular protection



Reduces workload of the heart by reducing myocardial O2 demand

Preserves K⁺ balance

Normalizes stress-induced systolic peaks with cardioselective beta-one blockade

Contraindicated in sinus bradycardia, heart block greater than first degree, cardiogenic shock, and overt cardiac failure.

Please consult Brief Summary of Prescribing Information on the following page.

Once-a-day in hypertension...

metoprolol tartrate



Changing the Course of Cardiovascular Care

Geigy

First-step protection for the hypertensive heart

Lopressor®

Ampuls Prefilled Syringes

BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE INSERT)

CONTRAINDICATIONS
Hypertension and Angina
Lopressor is contraindicated in sinus bradycardia, heart block
greater than first degree, cardiogenic shock, and overt cardiac
failure (see WARNINGS).

Myocardial Infarction

myocardial imarction
Lopressor is contraindicated in patients with a heart rate
< 45 beats/min; second- and third-degree heart block; significant first-degree heart block (P-R interval © 0.24 sec); systolic
blood pressure < 100 mmHg; or moderate-to-severe cardiac
faiture, (ss. WARDHING). blood pressure < 100 mi failure (see WARNINGS)

failure (see WARNINGS).

WARNINGS
Hypertension and Angina
Cardiac Failure: Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure. In hypertensive and angina patients who have congestive heart failure controlled by digitalis and diuretics, Lopressor should be administered cautiously. Both digitalis and Lopressor slow AV conduction.

In Patients Without a History of Cardiac Failure: Continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of impending cardiac failure, patients should be fully digitalized and/or given a diuretic. The response should be observed closely. If cardiac failure continues, despite adequate digitalization and diuretic therapy, Lopressor should be withdrawn.

Ischemic Heart Disease: Following abrupt cessation of therapy with certain beta-blocking agents, exacerbations of angina pectoris and, in some cases, myocardial infarction have occurred. When discontinuing chronically administered Lopressor, particularly in patients with ischemic heart disease, the dosage should be gradually reduced over a period of 1-2 weeks and the patient should be carefully monitored. If angina markedly worsens or acute coronary insufficiency develops, Lopressor administration should be reinstated promptly, at least temporarily, and other measures appropriate for the management of unstable angina should be taken. Patients should be warned against interruption or discontinuation of therapy without the physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue Lopressor therapy abruptly even in patients treated only for hypertension. Ischemic Heart Disease: Following abrupt cessation of abruptly even in patients treated only for hypertension

Bronchospastic Diseases: PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD. IN GENERAL, NOT RECEIVE
BETA BLOCKERS. Because of its relative beta; selectivity,
however, Lopressor may be used with caution in patients
with bronchospastic disease who do not respond to, or cannot tolerate, other antihypertensive treatment. Since beta;
selectivity is not absolute, a beta; stimulating agent should
be administered concomitantly, and the lowest possible dose
of Lopressor should be used. In these circumstances it would
be prudent initially to administer Lopressor in smaller dose
sthree times daily, instead of larger doses two times daily, to
avoid the higher plasma levels associated with the longer
dosino interval. (See DOSAGE AND ADMINISTRATION.) dosing interval. (See DOSAGE AND ADMINISTRATION.)

Major Surgery: The necessity or desirability of withdrawing beta-blocking therapy prior to major surgery is controversial; the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

Lopressor, like other beta blockers, is a competitive inhibitor Lopressor, like other beta blockers, is a competitive inhibited of beta-receptor agonists, and its effects can be reversed by administration of such agents, e.g., dobutamine or iso-proterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in restarting and maintaining the heart beat has also been reported with beta blockers.

blockers.

Diabetes and Hypoglycemia: Lopressor should be used with caution in diabetic patients if a beta-blocking agent is required. Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected.

Thyrotoxicosis: Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta blockade, which might precipitate a thyroid storm.

Myocardial Infarction

Myocardial Infarction
Cardiac Failure: Sympathetic stimulation is a vital component
supporting circulatory function, and beta blockade carries the
potential hazard of depressing myocardial contractility and precipitating or exacerbating minimal cardiac failure.
During treatment with Lopressor, the hemodynamic status
of the patient should be carefully monitored. If heart failure
occurs or persists despite appropriate treatment, Lopressor
should be discontinued.

should be discontinued. Bradycardia: Lopressor produces a decrease in sinus heart rate in most patients; this decrease is greatest among patients with high initial heart rates and least among patients with low initial heart rates. Acute myocardial infarction (particularly inferior infarction) may in itself produce significant lowering of the sinus rate. If the sinus rate decreases to < 40 beats/min, particularly if associated with evidence of lowered cardiac out-

put, atropine (0.25-0.5 mg) should be administered intra-venously. If treatment with atropine is not successful, Lopressor should be discontinued, and cautious administration of isoproterenol or installation of a cardiac pacemaker should

of soproterend or installation or a cardiac pacemaker should be considered. **AV Block:** Lopressor slows AV conduction and may produce significant first- (P-R interval ≥0.26 sec), second-, or third-degree heart block. Acute myocardial infarction also produces

heart block.

If heart block occurs, Lopressor should be discontinued and at heart block occurs, Lopressor should be discontinued and at the heart block occurs, Lopressor should be discontinued and the heart block. If treatment with atropine is not successful, cautious administration of isoproterenol or installation of a cardiac pacemaker should be considered.

Hypotension: If hypotension (systolic blood pressure Hypotension: If hypotension (systolic blood pressure 90 mmHg) occurs, Lopressor should be discontinued, and the hemodynamic status of the patient and the extent of myocardial damage carefully assessed. Invasive monitoring of central venous, pulmonary capillary wedge, and arterial pressures may be required. Appropriate therapy with fluids, positive inotropic agents, balloon counterpulsation, or other treatment modalities should be instituted. If hypotension is associated with sinus bradycardia or AV block, treatment should be directed at reversing these (see above).

Bronchospastic Diseases: PATIENTS WITH BRONCHO-SPASTIC DISEASES SHOULD, IN GENERAL, NOT RECEIVE BETA BLOCKERS. Because of its relative beta; selectivity, Lopressor may be used with extreme caution in patients with bronchospastic disease. Because it is unknown to what extent beta; stimulating agents may exacerbate myocardial

with bronchospastic disease. Because it is unknown to what extent beta_s-timulating agents may exacerbate myocardial ischemia and the extent of infarction, these agents should not be used prophylactically. If bronchospasm not related to congestive heart failure occurs, Lopressor should be discontinued. A theophylline derivative or a beta_a gonist may be administered cautiously, depending on the cilincal condition of the patient. Both theophylline derivatives and beta_a gonists may orduce serious cardiac arrivthmias. ists may produce serious cardiac arrhythmias.

PRECAUTIONS

General
Lopressor should be used with caution in patients with impaired hepatic function

paired hepatic function.
Information for Patients
Patients should be advised to take Lopressor regularly and continuously, as directed, with or immediately following meals. If a dose should be emissed, the patient should take only the next scheduled dose (without doubling it). Patients should not discontinue Lopressor without consulting the physician. Patients should be advised (1) to avoid operating automobiles and machinery or engaging in other tasks requiring alertness until the patient's response to therapy with Lopressor has been determined; (2) to contact the physician if any difficulty in breathing occurs: (3) to inform the physician or dentist before any type of surgery that he or she is taking Lopressor. Laboratory Tests

Laboratory Tests
Clinical laboratory findings may include elevated levels of serum transaminase, alkaline phosphatase, and lactate

dehydrogenase. **Drug Interactions**

Drug interactions
Catecholamine-depleting drugs (e.g., reserpine) may have an additive effect when given with beta-blocking agents. Patients treated with Lopressor plus a catecholamine depletor should therefore be closely observed for evidence of hypotension or marked bradycardia, which may produce vertigo, syncope, or postural hypotension.

therefore be closely observed for evidence of hypotension or marked bradycardia, which may produce vertigo, syncope, or postural hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility Long-term studies in animals have been conducted to evaluate carcinogenic potential. In 2-year studies in rats at three oral dosage levels of up to 800 mg/kp per day, there was no increase in the development of spontaneously occurring benign or malignant neoplasms of any type. The only histologic changes that appeared to be drug related were an increased incidence of generally mild focal accumulation of foamy macrophages in pulmonary alveoli and a slight increase in biliary hyperplasia. Neither finding represents symptoms of a known disease entity in man. In a 21-month study in Swiss albino mice at three oral dosage levels of up to 750 mg/kg per day, benign lung tumors (small adenomas) occurred more frequently in female mice receiving the highest dose than in untreated control animals. There was no increase in malignant or total (benign plus malignant) lung tumors, nor in the overall incidence of tumors or malignant tumors. This 21-month study was repeated in CD-1 mice, and no statistically or biologically significant differences were observed between treated and control mice of either sex for any type of tumor.

All mutagenicity tests performed (a dominant lethal study in mice, chromosome studies in somatic cells, a Salmonella/mammalian-microsome mutagenicity test, and a nucleus anomaly test in somatic interphase nuclei) were negative.

No evidence of impaired fertility due to Lopressor was observed in a study performed in rats at doses up to 55.5 times the maximum daily human dose of 450 mg. Distribution studies in mice confirm exposure of the fetus when Lopressor is administered to the pregnant animal. These studies have revealed no evidence of impaired fertility or teratogenicity. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of hu

Nursing mothers
Lopressor is excreted in breast milk in very small quantity. An infant consuming 1 liter of breast milk daily would receive a dose of less than 1 mg of the drug. Caution should be exercised when Lopressor is administered to a nursing woman.

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS
Hypertension and Angina
Most adverse effects have been mild and transient.

Central Nervous System: Tiredness and dizziness have occurred in about 10 of 100 patients. Depression has been reported in about 5 of 100 patients. Mental confusion and short-term memory loss have been reported. Headache, nightmares, and insomnia have also been reported. Headache, nightmares, and insomnia have also been reported. Cardiovascular: Shortness of breath and bradycardia have occurred in approximately 3 of 100 patients. Cold extremities; arterial insufficiency, usually of the Raynaud type; palpitations; congestive heart failure; peripheral edema; and hypotension have been reported in about 1 of 100 patients. (See CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS.)

Respiratory: Wheezing (bronchospasm) and dyspnea have been reported in about 1 of 100 patients (see WARNINGS).

Gastrointestinal: Diarrhea has occurred in about 5 of 100 patients. Nausea, dry mouth, gastric pain, constipation, flatulence, and heartburn have been reported in about 1 of 100 patients.

Hypersensitive Reactions: Pruritus or rash have occurred in about 6 of 100 patients.

Hypersensitive Reactions: Pruritus or rash have occurred in about 5 of 100 patients. Worsening of psoriasis has also been

reported.

Miscellaneous: Peyronie's disease has been reported in fewer than 1 of 100,000 patients. Musculoskeletal pain, blurred

vision, and tinnitus have also been reported.

There have been rare reports of reversible alopecia, agranulocytosis, and dry eyes. Discontinuation of the drug should be considered if any such reaction is not otherwise

explicable.

The oculomucocutaneous syndrome associated with the beta blocker practolol has not been reported with Lopressor.

Myocardial Infarction

myocardial inflaction Central Nervous System: Tiredness has been reported in about 1 of 100 patients. Vertigo, sleep disturbances, hallucina-tions, headache, dizziness, visual disturbances, confusion, and reduced libido have also been reported, but a drug rela-

tionship is not clear.

Cardiovascular: In the randomized comparison of Lopressor and placebo described in the CLINICAL PHARMACOLOGY section, the following adverse reactions were reported:

Looresson

Hypotension (systolic BP < 90 mmHg)	27.4%	23.2%
Bradycardia	15.9%	6.7%
(heart rate < 40 beats/min) Second- or	4.7%	4.7%
third-degree heart block First-degree	5.3%	1.9%
heart block (P-R ≥ 0.26 sec) Heart failure	27.5%	29.6%
Pagaigatague Ducanas of nulmo	nary origin has b	noon ro

Hespiratory: Dyspnea of pulmonary origin has been reported in fewer than 1 of 100 patients.

Gastrointestinal: Nausea and abdominal pain have been reported in fewer than 1 of 100 patients.

Dermatoling Park and the park of the park of

reported in fewer than 1 of 100 patients.

Dermatologic: Rash and worsened psoriasis have been reported, but a drug relationship is not clear.

Miscellaneous: Unstable diabetes and claudication have been reported, but a drug relationship is not clear.

Potential Adverse Reactions

Potential Adverse Reactions
A variety of adverse reactions not listed above have been reported with other beta-adrenergic blocking agents and should be considered potential adverse reactions to Lopressor.

Central Nervous System: Reversible mental depression progressing to catatonia, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Cardiovascular: Intensification of AV block (see CONTRA-INDICATIONS).

Hematologic: Agranulocytosis, nonthrombocytopenic pur-pura, thrombocytopenic purpura. Hypersensitive Reactions: Fever combined with aching and sore throat, laryngospasm, and respiratory distress.

OVERDOSAGE
Acute Toxicity
Several cases of overdosage have been reported, some leading

oral Lb₀s²s (mg/kg): mice, 1158-2460; rats, 3090-4670. Signs and Symptoms Potential signs and symptoms associated with overdosage with Lopressor are bradycardia, hypotension, bronchospasm, and

cardiac failure. **Treatment**

There is no specific antidote.

In general, patients with acute or recent myocardial infarc-tion may be more hemodynamically unstable than other pa-tients and should be treated accordingly (see WARNINGS, Myocardial Infarction).

On the basis of the pharmacologic actions of Lopressor, the following general measures should be employed:

Elimination of the Drug: Gastric lavage should be performed

penormed.

Bradycardia: Atropine should be administered. If there is no response to vagal blockade, isoproterenol should be administered cautiously.

Hypotension: A vasspressor should be administered. e.g..

Hypotension: A vasopressor snould be administered, e.g., levarterenol or dopamine.

Bronchospasm: A beta-stimulating agent and/or a theo-phylline derivative should be administered.

Cardiac Failure: A digitalis glycoside and diuretic should be administered. In shock resulting from inadequate cardiac contractility, administration of dobutamine, isoproterenol, or glucagon may be considered.

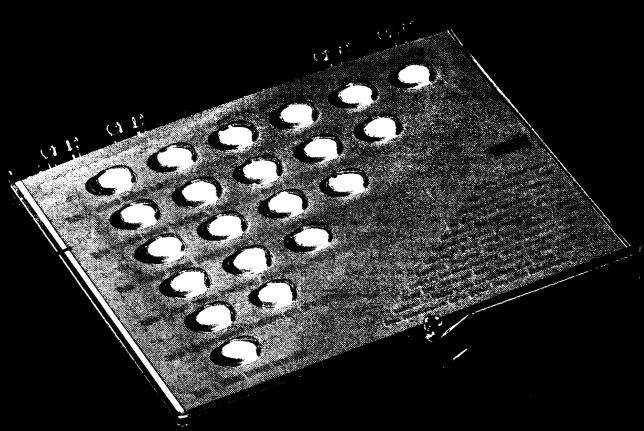


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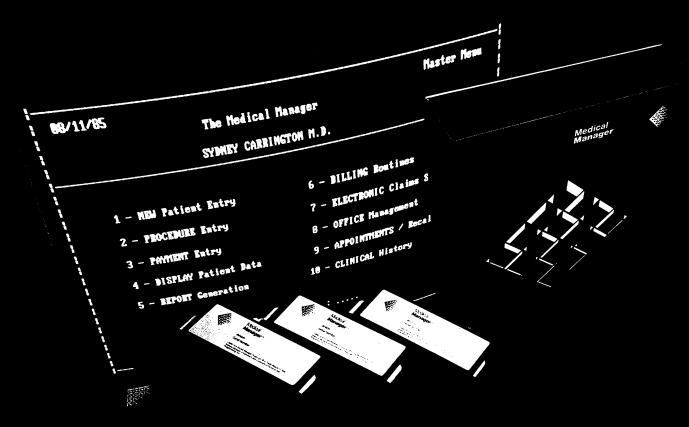
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CONTRAINDICATIONS: Anaphylactoid reactions have occurred in individuals hypersensitive to MOTRIN or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents.

WARNINGS: Peptic ulceration and G.I. bleeding, sometimes severe, have been reported. Ulceration, perfora-tion and bleeding may end fatally. An association has not been established. Use MOTRIN under close supervision in patients with a history of upper gastrointestinal tract disease, after consulting ADVERSE REACTIONS. In patients with active peptic ulcer and active rheumatoid arthritis, try nonulcerogenic drugs, such as gold. If MOTRIN is used, observe the patient closely for signs of ulcer perforation or G.I. bleeding.

PRECAUTIONS: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue MOTRIN and the patient should have an ophthalmologic examination including central visual fields and color vision testing.

Fluid retention and edema have been associated with MOTRIN; use with caution in patients with a history of cardiac decompensation or hypertension.

MOTRIN can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision, skin rash, weight gain, or edema.

Patients on prolonged corticosteroid therapy should have therapy tapered slowly when MOTRIN is added. The antipyretic, anti-inflammatory activity of MOTRIN may mask inflammation and fever

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of liver tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. Meaningful elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with ibuprofen as with other nonsteroidal anti-inflammatory drugs. If liver disease develops or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), MOTRIN should be discontinued.

In cross-study comparisons with 1200 mg to 3200 mg daily for several weeks, a slight dose-response de-crease in hemoglobin/hematocrit was noted. The total decrease in hemoglobin usually does not exceed 1 gram. Renal Effects: Long term administration of ibuprofen and other NSAID's to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome. In patients with prerenal conditions and reduced renal blood flow or blood volume, NSAID's may precipitate overt renal decompensation. Patients with impaired renal function, heart failure, liver dysfunction, those taking diuretics and the elderly are at greatest risk. Discontinuation of NSAID therapy is typically followed by recovery to the pretreatment state. In patients with renal impairment, reduced dosage may be necessary. Prospective studies of MOTRIN safety in patients with chronic renal failure have not been done.

Drug Interactions: Aspirin: Used concomitantly may decrease MOTRIN blood levels.

Coumarin: Bleeding has been reported in patients taking MOTRIN and coumarin.

ncy and nursing mothers: MOTRIN should not be taken during pregnancy or by nursing mothers. ADVERSE REACTIONS: The most frequent type of adverse reaction occurring with MOTRIN is gastrointestinal of which one or more occurred in 4% to 16% of the patients. Reported side effects were higher at 3200 than at 2400 mg/day or less.

Incidence Greater than 1% (but less than 3%) — Probable Causal Relationship

GASTROINTESTINAL: Nausea,* epigastric pain,* heartburn,* diarrhea, abdominal distress, nausea and
vomiting, indigestion, constipation, abdominal cramps or pain, fullness of GI tract (bloating and flatulence);
CENTRAL NERVOUS SYSTEM: Dizziness,* headache, nervousness; DERMATOLLOGIC: Rash* (including
maculopapular type), pruritus; SPECIAL SENSES; Tinnitus; METABOLIC/ENDOCRINE: Decreased appetite;
CARDIOVASCULAR: Edema, fluid retention (generally responds promptly to drug discontinuation; see

Incidence less than 1% Probable Causal Relationship**

GASTROINTESTINAL: Gastric or duodenal ulcer with bleeding and/or perforation, gastrointestinal hemorrhage, melena, gastritis, hepatitis, jaundice, abnormal liver function tests; CENTRAL NERVOUS SYSTEM:
Depression, insomnia, confusion, emotional lability, somnolence, aseptic meningitis with fever and coma;
DERMATOLOGIC: Vesiculobullous eruptions, urticaria, erythema multiforme, Stevens-Johnson syndrome,
alopecia; SPECIAL SENSES: Hearing loss, amblyopia (blurred and/or diminished vision, scotomata and/or
changes in color vision) (see PRECAUTIONS); HEMATOLOGIC: Neutropenia, agranulocytosis, aplastic anechanges in color vision) (see PRECAUTIONS); REMAIUDEN: Neutropenia, agranulocytosis, aplastic anemia, hemolytic anemia (sometimes Coombs positive), thrombocytopenia with or without purpura,
eosinophilia, decreases in hemoglobin and hematocrit (see PRECAUTIONS); CARDIOVASCULAR:
Congestive heart failure in patients with marginal cardiac function, elevated blood pressure, palpitations;
ALLERGIC: Syndrome of abdominal pain, fever, chills, nausea and vomiting; anaphylaxis pronchospasm
(see CONTRAINDICATIONS); RENAL: Acute renal failure in patients with pre-existing significantly impaired
renal function, decreased creatinine clearance, polyuria, azotemia, cystitis, hematuria; MISCELLANEOUS:

Decrease and mouth cincipal ulear, rhightie. Dry eyes and mouth, gingival ulcer, rhinitis.

Incidence less than 1%—Causal Relationship Unknown**

QASTROINTESTINAL: Pancreatitis; CENTRAL NERVOUS SYSTEM: Paresthesias, hallucinations, dream abnormalities, pseudotumor cerebri; DERMATOLOGIC: Toxic epidermal necrolysis, photoallergic skin reactions; SPECIAL SENSES: Conjunctivitis, diplopia, optic neuritis, cataracts; NEMATOLOGIC: Bleeding episodes (e.g. epistaxis, menorrhagia); METABOLIC/ENDOCRINE: Gynecomastia, hypoglycemic reaction, acidosis; CARDIOVASCULAR: Arrhythmias (sinus tachycardia, sinus bradycardia); ALLERGIC: Serum sickness, lupus erythematosus syndrome, Henoch-Schonlein vasculitis, angioedema; RENAL: Renal papillary necrosis.

*Reactions occurring in 3% to 9% of patients treated with MOTRIN. (Those reactions occurring in less than 3% of the patients are unmarked).

**Reactions are classified under "Probable Causal Relationship (PCR)" if there has been one positive rechallenge or if three or more cases occur which might be causally related. Reactions are classified under "Causal Relationship Unknown" if seven or more events have been reported but the criteria for PCR have not

OVERDOSAGE: In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine so alkaline diuresis may be beneficial.

DOSAGE AND ADMINISTRATION: Do not exceed 3200 mg/day.

Rheumatoid and osteoarthritis: Suggested dosage is 1200 to 3200 mg per day (400, 600 or 800 mg t.i.d. or q.i.d.). The smallest effective dosage should be used. Mild to moderate pain: 400 mg every 4 to 6 hours as

HOW SUPPLIED:

MOTRIN Tablets, 400 mg (orange) MOTRIN Tablets, 600 mg (peach) MOTRIN Tablets, 800 mg (apricot)
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Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum pot

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is meeded, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K* levels should be determined. If hyperkalemia develons, substitute a thiazide alone determined. If hyperkalemia develops, substitute a thiazide alone, restrict K* intake. Associated widened QRS complex or arrhythmia requires prompt additional therapy. Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions spen in adults. Thiazides appear and other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible

exacerbation or activation of systemic lupus erythematosus has

exacerbation or activation of systemic inpus et ginematusus das been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum polasicium levels. Huntever extensive clinical increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin converting been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin (ACTH)). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiszides should be used with caution in patients with impaired tenal function. The process of the control of the con precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in nation of the control agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to noreginephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolazizing muscle relaxants such as tubocyrarine reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly, Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, "Duazide's should be used with caution in natients with histories of association with the other usual calcinus components, interentre, Dyazide's bould be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following

hate incoming or dure measural reputing wave near reputing impotence has been reported in a lew patients on 'Dyazide'; a a causal relationship has not been established. Supplied: 'Dyazide' is supplied as a red and white cap in bottles of 1000 capsules; Single Unit Packages (un dose) of 100 (intended for institutional use only); in Patient-Pak' unit of-use bottles of 100. BRS-DZ:L42

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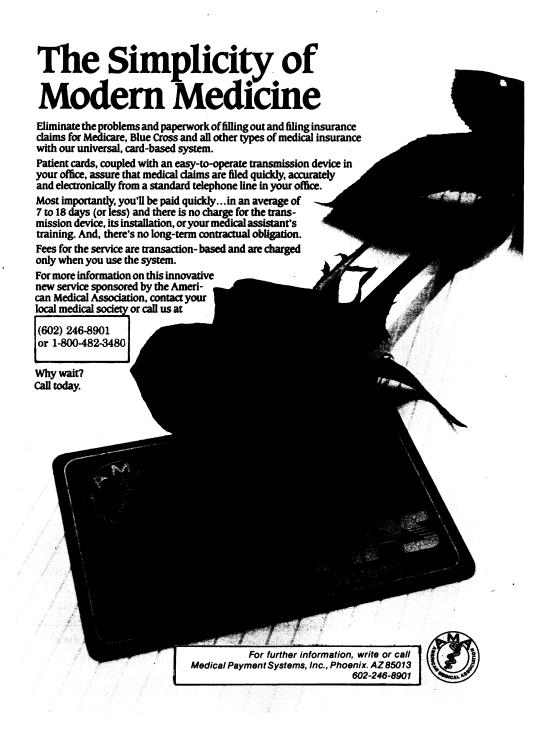
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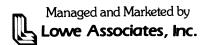
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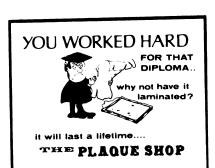
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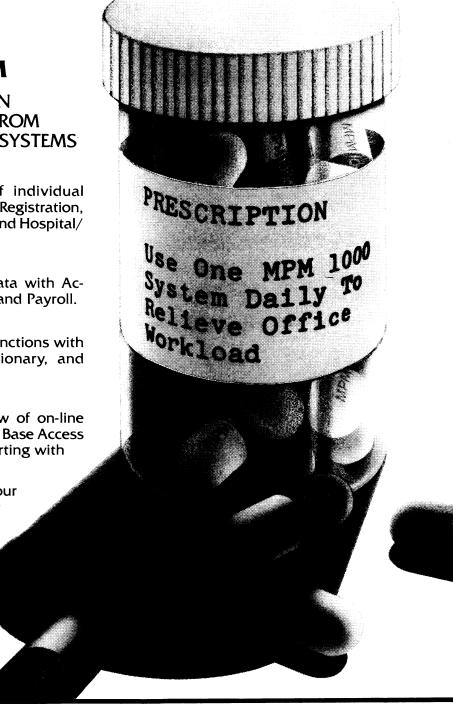
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PHYSICIANS WANTED

HEMATOLOGIST-ONCOLOGIST to join established multiethnic urban northern California private practice by August 1987. Second language of Mandarin, Cantonese, or Spanish necessary. Send CV and references. Please reply to Number 26, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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PHYSICIANS WANTED

SAN FRANCISCO

The San Francisco General Hospital AIDS Activities Division of the Department of Medicine of the University of California, San Francisco, is seeking applicants at the Assistant Clinical Professor level. Applicants should have completed a residency in Internal Medicine and be certified by the American Board of Internal Medicine. Additionally, applicants should have received post-residency training in General Internal Medicine or in a subspecialty relevant to AIDS such as Medical Oncology, Infectious Disease or Clinical Epidemiology. The individuals hired will be responsible for the care of AIDS patients, teaching on all levels, and are expected to participate actively in division research activities. Outpatient care is expected to be based in the SFGH AIDS Clinic. Inpatient care will be conducted at SFGH. Applicants should have demonstrated excellence in providing AIDS patient care and in medical teaching. Please submit current CV and three letters of reference to Paul Volberding, MD, Search Committee Chair, AIDS Activities Division, Building 80, Ward 84, San Francisco General Hospital, 995 Potrero Ave, San Francisco, CA 94110.

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CALIFORNIA, SAN FRANCISCO BAY AREA. A leading HMO near San Francisco, California is seeking Board prepared/certified physicians to staff a busy, urban, full-service Emergency Department. Kaiser Permanente is a large, pre-paid Health Maintenance Organization offering a competitive salary, job security, shareholder status, and generous benefits including health care, life insurance, disability insurance, sick leave, and educational leave. Please address all inquiries to Hans P. Odsen, MD, Chief, Emergency Department, Kaiser Permanente Medical Center, 1200 El Camino Real, South San Francisco, CA 94080; (415) 742-2513 or 2514.

DERMATOLOGIST. An expanding HMO in San Francisco is seeking a BC Dermatologist for a part-time position. Outpatient and inpatient responsibilities for consultations by referral. Send CV to Medical Director, PO Box 7883, San Francisco, CA 94120-9889.

WASHINGTON STATE, SEATTLE AREA. Multispecialty group of 9 physicians seeking OB/GYN and Family Practice physician for rapidly growing low risk practice. Community hospital located approximately 10 blocks from Clinic. Enumclaw is a family-oriented community, 50 miles from urban area and 60 minutes from outstanding ski resort. Send CV to Barbara Bellack, Clinic Manager, 3021 Griffin Ave, Enumclaw, WA 98022.

CHIEF OF PEDIATRICS. Natividad Medical Center, a University of California, San Francisco affiliated hospital, located in beautiful Monterey County, is seeking a BC/BE Pediatrician. Preference given to physician with Chief Residency or subspecialty experience. Natividad sponsors a family practice residency program with 18 residents. Salary range from \$73,000 to \$78,000 depen-3ing upon qualifications with excellent benefit package. Natividad Medical Center is an Affirmative Action Equal Opportunity Employer. For further information, please mail CV or contact Richard McClurkin, Personnel Officer/Search Board Leader, PO Box 8-1611, Salinas, CA 93912-1611; (408) 757-0581.

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(Continued on Page 782)



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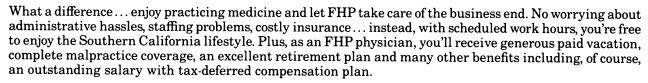
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(Continued from Page 778)

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ORTHOPEDIC SURGEON. Natividad Medical Center, a University of California, San Francisco affiliated hospital, located in beautiful Monterey County, is recruiting an Orthopedic Surgeon. This position combines teaching and practice. The hospital sponsors a family practice residency program with 18 residents and has a very active trauma service with a regional paramedic base station. An attractive base salary with fee-for-service incentive option is negotiable. Natividad Medical Center is an Affirmative Action Equal Opportunity Employer. For further information, please mail CV or contact: Richard McClurkin, Personnel Officer/Search Board Leader, PO Box 8-1611, Salinas, CA 93912-1611; (408) 757-0581.

EXCELLENT TEXAS OPPORTUNITIES. ENT, Family Practitioner, General Practitioner, General Surgeon, Internal Medicine, OB/GYN person, to practice in one of several lake area communities, in the beautiful Piney Woods area of east Texas. Enjoy boating, fishing, hunting year 'round. Excellent quality of life, first year guarantee, etc. Reply with CV to Medical Support Services, Armando L. Frezza, 11509 Quarter Horse Trail, Austin, TX 78750; (512) 331-4164.

PHYSICIANS WANTED

PYSCHIATRIST—BC/BE for northern California practice oriented towards clinical, occupational and evaluative medicine; qualified applicants will have EMG/NCS, EEG experience, be familiar with med-legal environment and seek a growth oriented opportunity; send current CV, letter of interest and compensation requirements to Box 164, 1550 California St, Ste 6, San Francisco, CA 94109.

MEDICAL DIRECTOR sought for women's nonprofit clinic in San Francisco. Responsibilities 80% clinical, 20% administrative. Emphases of the clinic include preventative health, outpatient gynecology, lesbian health care. Job is part-time, salary negotiable. Send CV with letter to Lyon-Martin Clinic, 2480 Mission St, #214, San Francisco, CA 94110. Deadline: June 30, 1987.

OREGON. Emergency department Medical Director and full-time Staff Physician are needed at client hospital located in community on the Columbia River in north central Oregon. Full service community hospital with moderate volume emergency department. Guaranteed rate of reimbursement, occurrence malpractice insurance coverage, CME allowance, reimbursement of professional dues, plus directors receive paid health benefits which include dependents. For additional information on this opportunity, contact Bill Salmo, Spectrum Emergency Care, 6275 Lehman Dr, Ste C202, Colorado Springs, CO 80918; 1 (800) 525-3681; (303) 590-1755.

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ORTHOPEDIC SURGEON. Full-time Orthopedic Surgeon to join growing multispecialty group in sunny California. Salary, incentive, malpractice and benefits. Great potential for right physician. Individual ownership. Send CV to Number 30, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

INTERNIST—Growing Long Beach, California industrial clinic seeks Internist to evaluate and treat Workers' Compensation patients. Position requires good communication skills and good patient rapport. No nights or weekends. Excellent benefits. Contact R. Unitan, 4237 Atlantic Ave, Long Beach, CA 90807; (213) 424-0423.

INTERNAL MEDICINE. Full-time BE/BC active Internist for multispecialty group in sunny California. Office/hospital and consult practice. Spanish a plus. Salary, benefits, and malpractice. Potential for partnership second year. Send CV to Number 31, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

(Continued on Page 789)

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- lowers blood pressure by reducing total peripheral resistance
- does not adversely affect heart rate and maintains cardiac output
- beta blockade minimizes risk of reflex tachycardia
- produces no adverse effect on HDL, cholesterol, or triglycerides
- does not impair renal function

...and supports your patients' life-styles

- maintains exercise capacity yet blunts surges in heart rate
- demonstrates a low incidence of impotence, fatigue, and cold extremities*

*Most adverse effects are mild, transient, and occur early in the course of treatment. In controlled clinical trials of three to four months' duration, the most common side effects noted in treating mild to moderate hypertension with NORMODYNE (labetalol HCI) Tablets include dizziness (11%), nausea (6%), and fatigue (5%). Dyspepsia (3%), nasal stuffiness (3%), impotence (1%), and drowsiness (<1%) have occurred to a lesser degree. Overall, reports of symptomatic postural hypotension have been uncommon and have included rare instances of syncope. For complete side effects profile, see Prescribing Information.

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BRIEF SUMMARY

INDICATIONS AND USAGE
NORMODYNE (labetald HCI) Tablets are indicated in the management of hypertension. NORMODYNE Tablets may be used alone or in combination with other antihypertensive agents, especially chiazide

CONTRAINDICATIONS
NORMODYNE (labetalol HCl) Tablets are contraindicated in bronchial asthma, overt cardiac failure, greater than first degree heart block,
cardiogenic shock, and severe bradycardia (see WARNINGS).

chial asthma, overt cardiac failure, greater than first degree heart block, cardiogenic shock, and severe bradycardia (see WARNINGS).

WARNINGS

Cardiac Failure Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure. Beta blockade carries a potential hazard of further depressing myocardial contractility and precipitating more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary, labetalol HCl can be used with caution in patients with a history of heart failure has been observed in patients receiving labetalol HCl. Labetalol HCl can be used with caution in patients with a history of heart failure has been observed in patients receiving labetalol HCl. Labetalol HCl does not abolish the inotropic action of digitalis on heart muscle.

In Patients Withou at History of Cardiac Failure In patients with latent cardiac insufficiency, continued depression of the myocardium with beta-blocket patients without a History of Cardiac Failure and the response observed closely. If cardiac failure continues, despite adquate digitalization and diunetic, NCRMODTNR (labetalol HCl) therapy should be withdrawn (gradually if possible).

Exacerbation of Ischemic Heart Disease Following Abrapy Withdrawal Angina pectors has not been reported upon labetalol HCl discontinuation. However, hypersensitivity to catecholamines has been observed in patients withdrawn from best-blocket retargy; exacerbation of angina and, in some cases, myocardial infarction have occurred after advapt discontinuation of such therapy. When discontinuation of such therapy, when discontinuation of such therapy. When discontinuation on Suph discontinuation of Such therapy. When discontinuation on ally diministered NORMODTNE (labetalol HCl), particularly in patients with incomic heart disease, the dosage should be gradually reduced over a period of one to two weeks and the patient should be carefully monitored. If majina markedly womens or accute coronary insufficiency

NORMODYNE (labetalol HC.1) therapy arruptny even in patients treated only for hypertension.

Nonallergic Bronchospasm (e.g., chronic bronchitis and emphysems) Patients with bronchospastic disease should, in general, not receive beta-blockers. NORMODYNE may be used with caution, however, in patients who do not respond to, or cannot tolerate, other anthypertensive agents. It is prudent, if NORMODYNE is used, to use the smallest effective dose, so that inhibition of endogenous or exogenous bera-anomiar is minimized.

amunipertensive agents. It is princed, it inconsisted to the smallest effective does, so that inhibition of endogenous or exogenous beta-agonists infinitised.

Pleochromocytoma Labetalol HCl has been shown to be effective in lowering the blood pressure and relieving symptoms in partients with pheochromocytoma. However, paradoxical hypertensive responses have been reported in a few patients with this tumor; therefore, use caution when administrating labetalol HCl to patients with pheochromocytoma. The prevent the appearance of premonitory signs and symptoms (e.g., tachycardia) of acute hypoglycemia. This is especially important with lable diabetics. Beta-blockade short or electronic products of the premonitory signs and symptoms (e.g., tachycardia) of acute hypoglycemia. This is especially important with lable diabetics. Beta-blockade short or electronic premonitors and the premonitor of the premonit

PRECAUTIONS

PRECAUTIONS
General Impaired Hepatic Function NORMODYNE (labetalol HCl)
Tablets should be used with caution in patients with impaired hepatic
function since metabolism of the drug may be diminished.

Jaundice or Hepatic Dysfunction On rare occasions, labetalol HCl
has been associated with jaundice (both hepatic and cholestatic). It is
therefore recommended that treatment with labetalol HCl be stopped
immediately should a patient develop jaundice or laboratory evidence of
liver injury. Both have been shown to be reversible on stopping therapy.

liver injury. Both have been shown to be reversible on stopping therapy. Information for Patients:

As with all drugs with beta-blocking activity, certain advice to patients being treated with labetalol HCI is warranted. This information is intended to all in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects. While no incident of the abrupt withdrawal phenomenon (exacerbation of angina pectoris) has been reported with labetalol HCI, dosing with NCRMODYNE Tablets should not be interrupted or discontinued without a physician's advice. Patients being treated with NORMODYNE Tablets should not be interrupted or discontinued failure. Also, transient scalp tingling may occur, usually when treatment with NORMODYNE Tablets is initiated (see ADVERSE REACTIONS).

Laboratory Tests

As with any new drug given over prolonged periods, laboratory parameters should be observed over regular intervals. In patients with concomitant illnesses, such as impaired renal function, appropriate tests should be done to monitor these conditions.

concomitant illnesses, such as impaired renal function, appropriate tests should be done to monitor these conditions. Drug Interactions

Drug Interactions

In one survey, 2.3% of patients taking labetalol HCl in combination with tricyclic antidepressants experienced tremor as compared to 0.7% reported to occur with labetalol HCl alone. The contribution of each of the treatments to this adverse reaction is unknown but the possibility of a drug interaction cannot be excluded.

Drugs possessing beta-blocking properties can blunt the bronchodilator effect of beta-receptor agonist drugs in patients with bronchospam; therefore, does greater than the normal anti-asthmatic does of beta-agonist bronchodilator drugs may be required.

Cimentiline has been shown to increase the bioavailability of labeta-lol HCl. Since this could be explained either by enhanced absorption or by an alteration of hepatic metabolism of labetalol HCl, special care should be used in establishing the dose required for blood pressure control in such patients.

Synengism has been shown between halothane anesthesia and intravenously administered labetalol HCl in association with halothane, high concentrations (3% or above) of halothane should not be used because the degree of hypotension will be increased enteral venous pressure. The anesthesiologist should be informed when a patient is receiving labetalol HCl.

Labetalol HCl blunts the reflex tachycardia produced by nitrogl erin without preventing its hypotensive effect. If labetalol HCl is us with nitroglycerin in patients with angina pectoris, additional antil pertensive effects may occur.

pertensive effects may occur.

Drug/Laboratory Test Interactions
The presence of a metabolite of labetalol in the urine may result in falsely increased levels of urinary catecholamines when measured by a nonspectific trihydroxyindole (THI) reaction. In screening patients superted of having a phechromocytoma and being treated with labetalol HCI, specific radioensymatic or high performance liquid chromatography assay techniques should be used to determine levels of catecholamines or their metabolites.

amines or their metabolites.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term oral dosing studies with labetalol HCl for 18 months in
mice and for 2 years in rats showed no evidence of carcinogenesis.

Studies with labetalol HCl, using dominant lethal assays in rats and
mice, and exposing microorganisms according to modified Ames tests,
showed no evidence of mutagenesis.

showed no evidence of mutagenesis.

Pregnancy Category C
leratogenic studies have been performed with labetalol in rats and rabbits at oral doses up to approximately 6 and 4 times the maximum commended human dose (MRHD), respectively. No reproducible evidence of fetal malformations was observed. Increased fetal resorptions were seen in both species at doses approximating the MRHD. There are no adequate and well-controlled studies in pregnant women. Labetalol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Notateratogenic Effects
Infants of mathem at the controlled studies in the potential of the potential based in the potential of the fetus.

Nonteratogenic Effects
Infants of mothers who were treated with labetalol HCl for hypertension during pregnancy did not appear to be adversely affected by the drug. Oral administration of labetalol to rats during late gestation through weaning at doses of 2 to 4 times the MRHD caused a decrease in neonatal survival.

Labor and Delivery
Labetalol HCl given to pregnant women with hypertension did not appear to affect the usual course of labor and delivery.

Supraise water the supraise of Pediatric Use Safety and effectiveness in children have not been establish

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Most adverse effects are mild, transient and occur early in the course of treatment. In controlled clinical trials of 3 to 4 months duration, discontinuation of NORMODYNE (labetalol HCI) Tablets due to one or more adverse effects was required in 7% of all patients. In these same trials, beta-blocker control agents led to discontinuation in 8 to 10% of patients, and a centrally acting alpha-agonist in 30% of patients. The incidence rates of adverse reactions listed in the following table were derived from multicenter controlled clinical trials, comparing labetalol HCI, placebo, metoprolol and propranolol, over treatment periods of 3 and 4 months. Where the frequency of adverse effects for labetalol HCI and placebo is similar, causal relationship is uncertain. The rates are based on adverse reactions considered probably drug-related by the investigator. If all reports are considered, the rates are somewhat higher (e.g., dizzines 20%, nauses 14%, fartigue 11%), but the overall conclusions are unchanged.

Labetalol HCl Placebo Propranolol Metoprolol

	(N = 227) %	(N = 98) %	(N = 84) %	(N = 49) %
Body as a whole				
fatigue	5 1 2	0	12	12
asthenia	1	- 1	1	0
headache	2	1	1	2
Gastrointestinal				
nausea	6	1	1	2 0 0 2 0
vomiting	<1	0	0	0
dyspepsia	3 <0 <1	1 0 0	1	0
abdominal pain	_0	Ō	1 2 0	2
diarrhea	<1	Ō	2	Ō
taste distortion	1		0	0
Central and Peripheral	Nervous Syst	ems		
dizziness	11	3	4	4
paresthesias	≨i	0	0 2	0
drowsiness		2	2	2
Autonomic Nervous Sy	stem			
nasal stuffiness	3	0 0 0	0 0 1 0	0 0 3 0
ejaculation failure	2	0	0	0
impotence	.1	0	1	3
increased sweating	<1	0	0	0
Cardiovascular				
edema	1	0	0	0
postural hypotension	1	ŏ	0 0 5	0
bradycardia	0	0	5	12
Respiratory				
dyspnea	2	0	1	2
Skin				
rash	1	0	0	0
Special Senses				
vision abnormality	1	0	0	0
vertigo	ž	ĭ	ŏ	ŏ
	1			•

The adverse effects were reported spontaneously and are representative of the incidence of adverse effects that may be observed in a properly selected hypertensive patient population, i.e., a group excluding patients with bronchospastic disease, overt congestive heart failure, or other contrandications to beta-blocker therapy.

Clinical trials also included studies utilizing daily doses up to 2400 mg in more severely hypertensive patients. Certain of the side effects increased with increasing dose as shown in the table below which depicts the entire U.S. therapeutic trials data base for adverse reactions that are clearly or possibly dose related.

Labetalol HCl Daily Dose (mg) Number of		200	300	400	600
Patients Dizziness (%)		522 2	181 3	606 3	608 3
Fatigue Nausea		<1	0	4	4 2
Vomiting Dyspepsia Paresthesias		1 2	0	<1 2 2	<1 1 2
Nasal Stuffiness Ejaculation Failure Impotence Edema		1 0 1 1	1 2 1 0	2 1 1 1	2 2 1 1
Labetalol HCl Daily Dose (mg) Number of	800	900	1200	1600	2400
Patients Dizziness (%) Fatigue	503 5	117 1 3	411 9 7	242 13 6	175 16 10
Nausea Vomiting Dyspepsia	<1 1	0	7 1 2	11 2 2	19 3 4

Labetalol HCl Daily Dose (mg) (cont.)	800	900	1200	1600	2400
Paresthesias	1	1	2	5	5
Nasal Stuffiness	2	Ž	4	5	6
Ejaculation Failure	3	0	4	3	5
Impotence	2	4	3	4	3
Edema	1	0	1	2	2

In addition, a number of other less common adverse events have been reported in clinical trials or the literature:
Cardiovascular Postural Mypotension, including rarely, syncope.
Central and Peripheral Nervous Systems Paresthesias, most frequent described as eagle trigling. In most cases, it was mild, transient and usually occurred at the beginning of treatment.
Collegen Disorders Systemic lupus erythematosus; positive antinuclear factor (ANF).
Ever Du eyes.

clear factor (ANF).

Eyes Dry eyes.

Immunological System Antimitochondrial antibodies.

Liwer and Bidary System Cholestasis with or without jaundice.

Musculo-Skeletal System Muscle cramps; toxic myopathy.

Respiratory System Bronchospasm.

Skin and Appendages Rashes of various types, such as generalized

maculo-papular; lichenoid; urticarial; bullous lichen planus; psoriafor
facial erythems; Peyronicé sliesses; reversible alopecia.

Urinary System Difficulty in micturition, including acute urinary
hadder retention.

bladder retention.

Following approval for marketing in the United Kingdom, a monitored release survey involving approximately 6,800 patients was conducted for further safety and efficacy evaluation of this product. Results of this survey indicate that the type, severity, and incidence of adverse effects were comparable to those cited above.

Potential Adverse Effects
In addition, other adverse effects not listed above have been
reported with other beta-adrenergic blocking agents.
Central Nervous System Reversible mental depression progressing to
catatonia; an acute reversible syndrome characterized by disorientation
for time and place, short-term memory loss, emotional lability, slightly
clouded sensorium, and decreased performance on neuropsychometrics.
Cardiovascular intensification of AV block. See
CONTRAINDICATIONS.
Allergic Fever combined with aching and sore throat; laryngospasm;
respiratory distress.
Hematologic Agranulocytosis: thresphorusosasia.

logic Agranulocytosis; thrombocytopenic or nonthrom-

remanding. Agrationer, young an observation of the bottopenic purpura.
Gastrointestinal Mesenteric artery thrombosis; ischemic colitis.
The oculomucocutaneous syndrome associated with the beta-blocker practold has not been reported with labetalol HCl.
Clinical laboratory tests: There have been reversible increases of serum transaminases in 48 of patients treated with labetalol HCl and tested, and more rarely, reversible increases in blood urea.

OVERDOSAGE

OVERDOSAGE

Overdosage with NORMODYNE (labetalol HCl) Tablets causes excessive bradycardia. Patients should be laid supine and their legs raised if necessary to improve the blood supply to the brain. The following additional measures should be employed if necessary: Excessive bradycardia—administer arropine (3.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously. Cardiac failure — administer adaptical adjuvence. Hypocension — administer vacopressors, e.g., norepinephrine. There is pharmacological evidence that norepinephrime may be the drug of choice. Bronchospasm — administer a betag-stimulating agent and/or a theophylline preparation.

Oastric lavage or pharmacologically induced emesis (using syrup of ipeacs) is useful for removal of the drug shortly after ingestion. Labetalol HCl can be removed from the general circulation by hemodialysis. The oral LDS you lose of labetalol HCl in the mouse is approximately 600 mg/kg and in the rat is greater than 2 gm/kg. The intravenous LDs0 in these species is 50 to 60 mg/kg.

in these species is 50 to 60 mg/kg.

DOSAGE AND ADMINISTRATION
DOSAGE MUST BE INDIVIDUALIZED. The recommended initial dose is 100 mg twice daily whether used alone or added to a diuretic regimen. After 2 or 3 days, using standing blood pressure as an indicator, dosage may be titrated in increments of 100 mg bid every 2 or 3 days.

The usual maintenance dosage of labetalol HCl is between 200 and 400 mg twice daily.

Since the full antihypertensive effect of labetalol HCl is usually seen within the first one to three hours of the initial dose or dose increment, the assurance of a lack of an exaggerated hypotensive response can be clinically established in the office setting. The antihypertensive effects of continued dosing can be measured at subsequent visits, approximately 12 hours after a dose, to determine whether further titration is necessary. Patients with severe hypertension may require from 1200 mg to 2400 mg per day, with or without thizaide diuretics. Should side effects (principally nausea or dizziness) occur with these doses administered bid, the same total daily dose administered there times daily may improve tolerability and facilitate further titration. Titration increments should not exceed 200 mg twice daily.

When a diuretic is added, an additive anthypertensive effect can be expected. In some cases this may necessitate a labetalol HCl dosage adjustment. As with most anthypertensive drugs, optimal dosages of NORMODYNE Tablets are usually lower in patients also receiving a diuretic.

When transferring patients from other antihypertensive drugs,

Muretic. When transferring patients from other antihypertensive drugs, When transferring patients from other antihypertensive drugs, NGRMODYNE Tablets should be introduced as recommended and the dosage of the existing therapy progressively decreased.

HOW SUPPLIED

HOW SUPPLIED

NORMODYNE (labetalol HCl) Tablets, 100 mg, light-brown, round, scored, film-coasted tablets engraved on noe side with Schering and product identification numbers 244, and on the other side the number 100 for the strength and "NRMODYNE"; bottles of 100 (NDC-008-0244-03), and box of 100 for unit-doe dispensing (NDC-008-0244-03), and box of 100 for unit-doe dispensing (NDC-008-0244-03), and box of 100 for unit-doe dispensing (NDC-008-0244-03), box of 100 for unit-doe dispensing (NDC-008-024-024-03), box of 100 for unit-doe dispensing (NDC-008-072-03), box of 100 for Unit-does dispensing (NDC-008-073-03), box of 100 for Unit-does of the strength and "NCRMODYNE"; bortles of 100 (NDC-008-0438-03), box of 100 for Unit-does dispensing (NDC-008-0438-02).

NORMODYNE (labetalol HCl) Tablets should be stored between 2* and 30°C (36* and 86*F).

NORMODYNE (labetalol HCl) Tablets in the unit-does boxes should be protected from excessive moisture.

For complete prescribing information, please consult package insert.

Schering Corporation Kenilworth, NJ 07033

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PHYSICIANS WANTED

FAMILY PRACTICE RESIDENCY DIRECTOR

The White Memorial Medical Center of Los Angeles is seeking an ABFP certified Family Physician to further develop a new and exemplary Family Practice Residency. A strong candidate will possess excellent clinical, teaching, administrative and leadership skills and will be eligible for California licensure.

This developing residency anticipates accepting residents in 1988. It has the academic sponsorship of the Loma Linda Medical School and the academic support of the University of Southern California Medical School, through the Hispanic Medical Education and Training (HISMET) Program.

Salary and benefits are fully competitive. An appropriate academic appointment is avail-

The White Memorial is an equal opportunity employer. Please send inquiries and résumés

> WMMC/HISMET Family Practice **Residency Program Department of Medical Education** White Memorial Medical Center 1720 Brooklyn Ave. Los Angeles, CA 90033

MULTISPECIALTY GROUP in San Francisco bay area looking for Board certified Family Practitioner for beautiful satellite office. Competitive salary and later incentive program. Contact David Louis, MD, 3100 Telegraph Ave, Oakland, CA 94609; (415) 273-8150.

WE HAVE FULL- AND PART-TIME LOCUM TE-NENS opportunities available with guaranteed incomes and paid malpractice. For more information, contact John Smith, Locum Tenens, Inc (A Division of Jackson and Coker), 400 Perimeter Center Terrace, Ste 760 WJM, Atlanta, GA 30346; Tel. 1 (800) 544-1987.

CLAYPOOL. Gila Medical Services Corporation seeks a Family Practice physician to provide medical care including OB and deliveries. Gila Medical Services operates a multispecialty group practice which provides routine primary medical care to the service area population of 29,000, with x-ray and lab services available on site. Salary and benefits commensurate with experience, with paid relocation expense. Claypool, Arizona is located almost equidistant from Phoenix and Tucson in Gila County. Reply to AHPR, 3131 E. Second St, Tucson, AZ 85716; (602) 626-7946.

WASHINGTON STATE

The Wenatchee Valley Clinic, a multispecialty group of 105 physicians, has several practice opportunities throughout its seven practice locations. Currently we are seeking:

MAIN FACILITY—WENATCHEE

- Pediatrics
- Psychiatry
- AllergyNephrology
- General Internal Medicine
- SATELLITE FACILITIES—OMAK/MOSES LAKE
 - Orthopedics OB/GYNRadiology
 - **General Surgery**
 - General Internal Medicine

All positions offer an excellent compensation and benefit package. North central Washington provides a high quality of life for those interested in an abundance of recreational opportunities in a family-oriented rural setting. If interested, send your CV to Dr Gerald Gibbons, Medical Director, Wenatchee Valley Clinic, 820 N. Chelan Ave, Wenatchee, WA 98801, or call (509) 663-8711, ext 205.

PHYSICIANS WANTED

Western States OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 300 positions of various specialties.

Western States Physician Services 407 S. Clovis Ave, Ste 108 Fresno, CA 93727; (209) 252-3000

NORTHERN CALIFORNIA, EMERGENCY MEDI-CINE. Full-time positions available in the Emergency Department at the University of California, Davis, Medical Center. The University serves a large region of northern California and is a major trauma center. Emergency physicians teach and supervise medical students and housestaff (240 per year) in addition to treating patients. Emergency Department physicians also provide medical control for UCDMC Life Flight, director of base station activities, and are actively involved in trauma care. Opportunities exist for involvement in other UCD School of Medicine teaching activities. Applicants should send CV to Robert W. Derlet, MD, Chief, Division of Emergency Medicine, University of California, Davis, Medical Center, 2315 Stockton Blvd. Sacramento, CA 95817

NEAR SAN FRANCISCO BAY AREA. Board eligible Internist to join 4 other Internists in private practice covering rural ER/Acute Medicine. Involves four two-night shifts per month. Scheduling flexible. Sense of humor preferred. 60K per year. Charles Rath, MD, 199 E. Webster St, Colusa, CA 95932; (916) 458-7739.

DIRECTOR OF NEW INTENSIVE CARE UNIT, MEDICAL-SURGICAL. BC in major specialty, preferably Medicine, Surgery, or Anesthesiology is required with additional qualifications and experience desired. Prefer person who enjoys teaching and works well with nursing and medical staff. Minimum salary guarantee with time and opportunity for additional related practice. Kaweah Delta District Hospital is a 278-bed community hospital that is a major trauma and regional cancer center. Located in Visalia, California, a small business and agricultural community in the San Joaquin Valley of central California. Submit letter and recent CV to David L. Roberts, MD, Director of Medical Education, Kaweah Delta District Hospital, 400 W. Mineral King, Visalia, CA 93291; (209) 625-7308.

PATHOLOGIST. Associate needed for two-man group in southern California, 250-bed community hospital. Please send CV and pertinent references at first contact. \$60,000-80,000 salary range depending on qualifications. Please contact Pathologist, PO Box 3249, Bakersfield, CA 93385.

WYOMING. Part-time position available in Lander, Wyoming for an ABEM certified/prepared Emergency Physician in low ED at Lander Valley Regional Medical Center. Have time to enjoy skiing, climbing, fishing, and camping in the Wind River Mountains, Tetons, and Yellowstone. Contact Wind River Emergency Physicians, PO Box 463, Lander, WY 82520.

NEUROLOGIST. An expanding HMO in San Francisco is seeking a BC Neurologist for a part-time position. Outpatient and inpatient responsibilities for consultations by referral. Send CV to Medical Director, PO Box 7883, San Francisco, CA 94120-9889

Ads Get Results!

CLASSIFIED INFORMATION (415) 863-5522 EXTENSION 244

PHYSICIANS WANTED

SAN DIEGO, CALIFORNIA. Career opportunities for full-time Family Practitioners and Internists with expanding network of ambulatory care centers. Send CV in confidence to Mercy CarePoint Medical Group, 681 Encinitas Blvd, Ste 406-W, Encinitas, CA 92024.

SAN DIEGO

Growing, well-established multispecialty group in San Diego seeks well-trained Family Physician, Pediatri-Diego seeks well-trained Family Physician, Pediatrician, General Internist and Cardiologist to join in the group's expansion and enjoy a quality life-style. For further information and consideration, please forward CV to Miriam Stephens, Director/Professional Recruitment at: SMITH HANNA MEDICAL GROUP, 5703 Oberlin Dr. #302-49, San Diego, CA 92121.

LAKE HAVASU CITY. Immediate opportunity available for BE/BC Internist with subspecialty interest in Cardiology to establish private practice. Excellent practice potential for committed, active practitioner. Havasu Regional Hospital is willing to provide some start-up assistance. Lake Havasu City is located on the Colorado River where recreational activities abound. Reply to AHPR, 3131 E. Second St, Tucson, AZ 85716; (602) 626-7946.

MINNEAPOLIS. Seeks BC/BE associates in Adult Psychiatry, Cardiology, Family Practice, Internal Medicine, Obstetrics and Gynecology and Urology. Practice quality medicine in a prepaid multispecialty setting located in one of America's leading metropolitan areas. Comprehensive benefits, excellent facilities, flexible compensation programs. For further information about joining the Group Health medical staff, call Jerry Hess at (612) 623-8444 or write to Group Health, Inc, Attn: Jerry Hess, 2829 University Ave, SE, Minneapolis, MN 55414

FAMILY PRACTICE. Excellent professional opportunity in beautiful north Idaho. Nominal lease at hospital owned clinic includes fully-equipped office, treatment suites and general receptionist. X-ray, lab and pharmacy on site. Located in 4season playground rich with recreational opportunities. For information call Nancy at (208) 784-1221, ext 304, or send résumé to Shoshoné Medical Center, Jacobs Gulch, Kellogg, ID 83837

BC OR BE ORTHOPEDIC SURGEON wanted to join medical group in northern California. Beautiful facility, professional staff, offering an opportunity for both professional growth and stimulation with guaranteed salary, plus malpractice, health insurance, two weeks paid vacation the first year and a partnership percentage thereafter. Serious applicants please contact (916) 689-2040.

PSYCHIATRIST. Immediate position with Kern County Mental Health Department (Bakersfield, California). \$57K to \$73K. Requires California license (or eligibility) to practice medicine and 3 years residency in approved Psychiatry Program. Please contact Mr Ed Rous, Director, Kern County Mental Health Department, 1960 Flower St, Bakersfield, CA 93305; (805) 861-2251.

GENERAL SURGEON. Excellent opportunity for BC/BE in General Surgery. Close to San Francisco in beautiful wine country. Reply to Number 38, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

EXCELLENT TEXAS OPPORTUNITIES. General Surgeon, Internal Medicine, OB/GYN, Pediatrician, to practice in a community close to Houston. Enjoy country living at its best with the convenience of Houston within 40 minutes. New hightech 150-bed hospital with good x-coverage, excellent quality of life. First year guarantee, etc. Reply with CV to Medical Support Services, Armando I Frezza, 11509 Quarter Horse Trail, Austin, TX 78750; (512) 331-4164.

(Continued on Page 790)

(Continued from Page 789)

PHYSICIANS WANTED

CALIFORNIA FORENSIC MEDICAL GROUP, INC, a corporation providing medical services in California county jails, has opportunities for physicians with a specialty in either Family Practice, General Practice or Internal Medicine. Send résumé to CFMG, Inc, PO Box 1831, Salinas, CA 93902; or contact Elaine Hustedt (408) 422-0214.

CALIFORNIA, SAN FRANCISCO BAY AREA. Full-time career Emergency Physician wanted for high-volume Emergency Department. Emergency Medicine Board certified or Board-ready mandatory to participate in a group of 20 full-time staff physicians seeing over 300 patients per day. Salaried position, excellent benefits include three weeks paid vacation; one week CME; paid malpractice, health and life insurance; corporate shareholdership in three years. Send CV or contact David Gallagher, MD, 27400 Hesperian Blvd, Hayward, CA 94545.

ARIZONA-BASED PHYSICIAN recruiting firm has opportunities coast-to-coast. "Quality Physicians for Quality Clients since 1972." Call (602) 990-8080; or send CV to Mitchell & Associates, Inc, PO Box 1804, Scottsdale, AZ 85252.

FAMILY PHYSICIAN. Residency trained, BC/BE. Currently a four-doctor group. Need to replace female partner who is leaving June 1987. OB optional. Current partners are also clinical faculty, UC Davis. Excellent community and hospital. Woodland is 15 miles from Sacramento and Davis. Contact J. T. Barrett, MD, W. J. Blevins Medical Center, 3 Court St, Woodland, CA 95695.

FAMILY PRACTICE/INTERNAL MEDICINE/ENDOCRINOLOGY/CARDIOLOGY/OCCUPATIONAL MEDICINE physicians, BC/BE needed immediately to join expanding multispecialty group. Practice in rapidly growing southwest community (population 500,000 plus). Fee-for-service and prepaid health care. Group includes Family Practice/Pediatrics/Internal Medicine/Subspecialties/24-hour Urgent Care. Teaching appointment. Position offers excellent compensation and benefits plus full pension and profit sharing. Relocation expenses. Interested individuals should reply with CV to Southwest Medical Associates, PO Box 15645, Las Vegas, NV 89114-5645.

WYOMING—EMERGENCY MEDICINE. Immediate opening. Full-time ER Physician. Pleasant working conditions. New hospital. Competitive compensation. Flexible scheduling. Paid malpractice. Small community life-style. Excellent outdoor recreation: camping, hunting, fishing, skiing and more. 72 miles to Salt Lake City. Send CV to Steven P. French, MD, Director, Emergency Department, 190 Arrowhead Dr, Evanston, WY 82930; (307) 789-3636.

WORK PART-TIME. Position available for Internist or GP/FP with Internal Medicine experience in Primary Care Practice, northern California Sierra foothills community of 25,000. Share rotating practice with two other MDs; you work one week in three. Outpatient and inpatient responsibilities (no OB, no ICU) in modern, fully-equipped 100-bed hospital. Minimum salary of \$1,800/week (with incentives, actual will be around \$2,200/week). Insurance, housing, and meals provided N/C. Send CV to David Lomba, 133 'B' Ascot Ct, Moraga, CA 94556.

SACRAMENTO AREA. Radiology. Interesting multioffice practice. Part-time and vacation coverage needed. Possible long-term association. Robert Swisher, MD, 729 Sunrise Ave—901, Roseville, CA 95661; (916) 786-9440.

PHYSICIAN OPENING. Ambulatory care/minor emergency center. Full- or part-time for FP/IM/EM trained/experienced physician. Located in Tacoma area. Flexible scheduling, pleasant setting, quality medicine. Contact David R. Kennel, MD, 5900-100th St SW, Ste 31, Tacoma, WA 98499; (206) 584-3023 or (206) 582-2542.

PHYSICIANS WANTED

PACIFIC NORTHWEST Rapidly Growing, Low Risk Practice Beautiful Country Setting

Eight-person group seeks second OB/GYN to meet increased demand. 38-bed hospital equipped for mammography, ultrasound, and laparoscopy. Family-oriented community with easy access to Seattle and prime ski resort. Contact:

The Friedrich Group, Inc. 9284 Ferncliff Northeast Bainbridge Island, WA 98110 (206) 547-7850 or (206) 842-5248

THE IRVINE MEDICAL CENTER and the University of California, Irvine, Department of Radiological Sciences are seeking a full-time faculty member for the Department of Radiological Sciences at the Clinical Assistant or Associate Professor level who would be assigned as Director of the Department of Radiology at Irvine Medical Center. The Irvine Medical Center is a new 177-bed hospital currently under construction in Irvine, California. Hospital opening is scheduled for fall of 1988. Administrative experience and academic background, including teaching and/or research, are required. Please send CV and the names of five references to Richard M. Friedenberg, MD, Professor and Chairman, Department of Radiological Sciences, University of California, Irvine, 101 City Dr South, Orange, CA 92668. The University of California is an affirmative action and an equal opportunity employer.

CENTRAL WASHINGTON STATE. Ambulatory care center seeks Primary Care Physician for full-time position. This challenging career opportunity offers a competitive salary/benefit package, interesting work, and adequate time off to enjoy the area's scenic beauty and abundant recreation. Contact Number 35, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

CALIFORNIA, MERCED. Emergency Department medical directorship and full-time staff opportunities are available at our client hospital in Merced. Full-service community hospital with moderate volume ED. Guaranteed rate of compensation, occurrence malpractice insurance coverage, CME allowance, reimbursement of professional dues, relocation allowance. Must be willing to live in community. For additional details contact Bill Salmo, Spectrum Emergency Care, 6275 Lehman Dr, Ste C-202, Colorado Springs, CO 80918; 1 (800) 525-3681; (303) 590-1755.

MEDICAL OFFICER (OCCUPATIONAL MEDICINE). GM-602-13, salary range \$47,911 to \$59,268; Naval Medical Clinic, Occupational Medical Branch, Port Huerieme, California; send résumés to NCBC, Code 231 (M. Presley), Bldg 14, Rm 157, Port Hueneme, CA 93043-5000; or call (805) 982-4473.

CASA GRANDE. Family Health Center in community with new 100-bed hospital, located between Phoenix and Tucson needs dynamic Family Practice physician (BC/BE) willing to do OB and deliveries. Guaranteed first year salary, bonus and paid malpractice insurance, four weeks paid vacation. Send CV to AHPR, 3131 E. Second St, Tucson, AZ 85716; (602) 626-7946.

INTERNAL MEDICINE. San Francisco suburb. BC/BE associate needed for busy solo practice adjacent to Mount Diablo Hospital. Send CV to Number 41, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

INTERNIST position available with 35 member multispecialty group; BC/BE; immediate opening; full range of benefits plus immediate shareholder status; excellent opportunity; central coast of California. Respond with CV to Colin J. Wells, MD, San Luis Medical Clinic, Ltd, 1235 Osos St, San Luis Obispo, CA 93401-3619. NO PHONE CALLS PLEASE.

PHYSICIANS WANTED

PSYCHIATRIC RESIDENT. Specific duties involve taking medical and psychiatric histories, performing physical examinations, establishing diagnoses, and designing and implementing treatment plans as a psychiatric resident. Job entails the clinical practice of medicine in a university teaching institution under careful supervision. MD degree required. Position is full-time with additional evening and weekend on call responsibilities. Salary: \$17,650 per annum. Apply by résumé (Reference Job Order #328764) to Job Services, PO Box 829, Fargo, ND 58107.

MONTANA. Emergency Physician needed in expanding ER group in the beautiful Bitterroot Valley of western Montana. Contact Jim Hansen, MD, PO Box 1262, Hamilton, MT 59840; (406) 363-2526.

SITUATION WANTED

INTERNIST. Board certified in Internal Medicine, desires full-time employment with group or HMO. Physician also has subspecialty of Oncology and Hematology. Will practice primary care Internal Medicine and/or Oncology and Hematology. Also interested in position of medical or hospital administrator. Physician has private practice and HMO experience. Site must be within 45 minutes or 25 miles of Long Beach, California. Available May 1987. Please call David Dworkin, MD, at (213) 494-7473 or (714) 722-6926 or write to 6250 Majorca Cir, Long Beach, CA 90803.

EXPERIENCED NEUROLOGIST, BC, with 4 years' experience performing and interpreting MRI and CT of head and spine as well as carotid ultrasound. Seeks affiliation with group needing expertise in these areas. Reply to Number 39, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

LOCUM TENENS

LOCUM TENENS PATHOLOGIST AVAILABLE. Board certified AP/CP, experienced. Previous clinical experience. US graduate. Prefer 1 month or longer. References upon request. Reply to Number 40, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

LOCUM TENENS, INC. (A Division of Jackson and Coker), can staff your practice from 2 weeks to 52 weeks, malpractice insurance for all 50 states, contact John Smith, 400 Perimeter Center Terrace, Suite 760 WJM, Atlanta, GA 30346; Tel. 1 (800) 544-1987.

LOCUM TENENS SERVICE WESTERN PHYSICIANS REGISTRY

... offers coverage for vacation or continuing education. To arrange coverage for your practice or to participate as temporary physician, contact: Carol Sweig, Director, 1315 Evans Ave, San Francisco, CA 94124; (415) 826-7676.



CLASSIFIED INFORMATION
(415) 863-5522 EXTENSION 244

In mild to moderate hypertension







JAMES B.

38, black male, heavy smoker. Prescribed a diuretic by another physician last year for hypertension.

YOUR CONCERNS Presents with "smoker's cough." Workup reveals a BP of 150/107.

A LOGICAL CHOICE FOR CONTROL OF HIS BP ISOPTIN* (verapamil HCI/Knoll) because...

 Black hypertensives often have low plasma renin activity and generally do not respond favorably to beta blockers.

 Beta blockers may increase the likelihood of bronchospasm.

ALICE W.

65, diabetic, overweight. Her BP has elevated to 190/98.

YOUR CONCERNS She's on daily insulin.

A LOGICAL CHOICE FOR CONTROL OF HER BP ISOPTIN* (verapamil HCI/Knoll) because...

 Unlike most beta blockers and diuretics, ISOPTIN has no adverse effects on serum glucose levels.

Unlike most beta blockers, ISOPTIN does not mask the symptoms of hypoglycemia.





THOMAS G.

70, asthmatic. In the past, BP adequately controlled with 25 mg hydrochlorothiazide daily.

YOUR CONCERNS

Today patient presents with symptoms of gout. Workup reveals high uric acid level, low serum potassium, and BP elevated to 180/98.

A LOGICAL CHOICE FOR CONTROL OF HIS BP ISOPTIN* (verapamil

HCI/Knoll) because...

— Unlike diuretics, ISOPTIN will not decrease serum potassium levels or elevate uric acid levels.

 Unlike beta blockers, ISOPTIN can be used safely in asthma and COPD patients.

JOHN K.

42, Annual physical uncovered diastolic BP of 102... confirmed on three successive office visits. Unresponsive to nonpharmacologic intervention.

YOUR CONCERNS

Salesman, spends many hours of his working day in car... total cholesterol level 300, HDL 35.

A LOGICAL CHOICE FOR CONTROL OF HIS BP

ISOPTIN' (verapamil HCI/Knoll) because...

— Unlike diuretics, ISOPTIN does not cause urinary urgency.

 Unlike either beta blockers or diuretics, ISOPTIN will not adversely affect his already seriously compromised lipid profile.

 Unlike with propranolol, fatigue and impotence are rarely reported.



Antihypertensive therapy you and your patients can live with







In mild to moderate hypertension THE FIRST ONCE DAILY CALCIUM CHANNEL BLOCKER

ISOPTIN° SR (verapamil HCI/Knoll) 240 mg scored, sustained-release tablets

CONTRAINDICATIONS: 1) Severe left ventricular dysfunction (see WARNINGS), 2) Hypotension (less than 90 mmHg systolic pressure) or cardiogenic shock, 3) Sick sinus syndrome or 2nd or 3rd degree AV block (except in patients with a functioning artificial ventricular pacemaker).

Brief Summary

WARNINGS: Heart Failure: ISOPTIN should be avoided in patients with severe left ventricular dysfunction (see DRUG INTERACTIONS). Patients with milder ventricular dysfunction should, if possible, be controlled before verapamil treatment. Hypotension: ISOPTIN (verapamil HCl) may produce occasional symptomatic hypotension. Elevated Liver Enzymes: Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported. Periodic monitoring of liver function in patients receiving verapamil is therefore prudent. Accessory Bypass Tract (Wolff-Parkinson-White): Patients with paroxysmal and/or chronic atrial flutter or atrial fibrillation and a coexisting accessory AV pathway have developed increased antegrade conduction across the accessory pathway producing a very rapid ventricular response or ventricular fibrillation after receiving intravenous verapamil as the verapamil of the pathway producing a very rapid usually D.C.-cardioversion. Atrioventricular Block: The effect of verapamil on AV conduction and the SA node may cause asymptomatic 1st degree AV block and transient bradycardia. Higher degrees of AV block, while infrequent (0.8%), may require a reduction in dosage or, in rare instances, discontinuation of verapamil HCl. Patients with Hypertrophic Cardiomyopathy (HHSS): Although verapamil has been used in the therapy of patients with IHSS, severe cardiovascular decompensation and death have been noted in this patient population.

PRECAUTIONS: Impaired Hepatic or Renal Function: Verapamil is highly metabolized by the liver with about 70% of an administered dose excreted in the urine. In patients with impaired hepatic or renal function verapamil should be administered cautiously and the patients monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacological effects (see OVERDOSAGE).

Drug Interactions: Beta Blockers: Concomitant use of ISOPTIN and oral beta-adrenergic blocking agents may be beneficial in certain patients with chronic stable angina or hypertension, but available information is not sufficient to predict with confidence the effects of concurrent treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities. Digitalis: Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted. However, chronic verapamil treatment increases serum digoxin levels by 50 to 75% during the first week of therapy and this can result in digitalist toxicity. Upon discontinuation of ISOPTIN (verapamil HCl), the patient should be reassessed to avoid underdigitalization. Antihypertensive Agents: Verapamil administered concomitantly with oral antihypertensive agents (e.g., vasodilators, angiotensin-converting enzyme inhibitors, diuretics, beta blockers, prazosin) will usually have an additive effect on lowering blood pressure. Patients receiving these combinations should be appropriately monitored. Dispoyramide: Disopyramide should not be administered within 48 hours before or 24 hours after verapamil administration. Quinidine: In patients with hypertrophic cardiomyopathy (IHSS), concomitant use of verapamil and quinidine resulted in significant hypotension. There has been a report of increased quinidine levels during verapamil therapy. Nitrates: The pharmacologic profile of verapamil and nitrates as well as clinical experience suggest beneficial interactions. Cimetidine: Two clinical trials have shown a lack of significant verapamil interaction with cimetidine. A third study showed cimetidine reduced verapamil clearance and increased elimination to 1/2. Anesthetic Agents: Verapamil may potentiate the activity of neuromuscular blocking agents and inhalation anesthetics. Carbamazepine: Verapamil may increase carbamazepine concentrations during combined therapy. Ritampin: Therapy with ritampin may marked

ADVERSE REACTIONS: Constipation 8.4%, dizziness 3.5%, nausea 2.7%, hypotension 2.5%, edema 2.1%, headache 1.9%, CHF/pulmonary edema 1.8%, fatigue 1.7%, bradycardia 1.4%, 3° AV block 0.8%, flushing 0.1%, elevated liver enzymes (see WARNINGS). The following reactions, reported in less than 1.0% of patients, occurred under conditions (open trials, marketing experience) where a causal relationship is uncertain; they are mentioned to alert the physician to a possible relationship: angina pectoris, arthralgia and rash, AV block, blurred vision, cerebrovascular accident, chest pain, claudication, confusion, diarrhea, dry mouth dyspnea, ecchymosis or bruising, equilibrium disorders, exanthema, gastrointestinal distress, gingival hyperplasia, gynecomastia, hair loss, hyperkeratosis, impotence, increased urination, insomnia, macules, muscle cramps, myocardial infarction, palpitations, paresthesia, psychotic symptoms, purpura (vasculitis), shakiness, somnolence, spotty menstruation, sweating, syncope, urticaria. Treatment of Acute Cardiovascular Adverse Reactions: Whenever severe hypotension or complete AV block occur following oral administration of verapamil, the appropriate emergency measures should be applied immediately, e.g., intravenously administered isoproterenol HCl, levarterenol bitartrate, atropine (all in the usual doses), or calcium gluconate (10% solution). If further support is necessary, inotropic agents (dopamine or dobutamine) may be administered. Actual treatment and dosage should depend on the severity and the clinical situation and the judgment and experience of the treating physician.

OVERDOSAGE: Treatment of overdosage should be supportive. Beta-adrenergic stimulation or parenteral administration of calcium solutions may increase calcium ion flux across the slow channel, and have been used effectively in treatment of deliberate overdosage with verapamil. Clinically significant hypotensive reactions or fixed high degree AV block should be treated with vasopressor agents or cardiac pacing, respectively. Asystole should be handled by the usual measures including cardiopulmonary resuscitation.

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PART-TIME MEDICAL CONSULTANT CONTRACTS

Physicians needed to work under contract, on a part-time basis for the Social Security Administration's Disability Insurance Program. Involves review of medical evidence in disability claims at 100 Van Ness Avenue, San Francisco, California. No patient contact. Applicants must: (1) have a valid license to practice medicine in the USA; (2) have recent or current clinical experience; and (3) be available between 7:00 a.m. and 4:30 p.m., Monday through Friday for case review. Subject to change, the specialties needed are Cardiology, Pulmonary Medicine, Psychiatry and Neurology. In addition to physicians for medical review, a chief medical consultant (Regional Medical Advisor) is needed. This is an administrative position and, in addition to the above criteria, one year's experience in the Disability Programs Branch is required. Applicants for this position should be available approximately 20 hours per week. Women and minorities are encouraged to apply. If interested in applying please submit a current curriculum vitae by July 15, 1987 to the address shown below. The curriculum vitae should address the following selection factors:

Selection Criteria

1. Medical Training

Identity specialty, training facility, dates, and number of years in specialty. Please indicate if you are Board eligible or certified and in what specialty.

2. Medical Experience (Current and Past)

- A. Clinical Practice
 - Identify dates, location and nature of clinical practice and experience and whether full time or part time.
- B. Other Experience

Identify other professional activities and experience such as teaching, publications, involvement with committees and professional organizations, etc.

- 3. Disability Claims Experience, reviewing evidence of record in order to evaluate claims for benefits:
 - A. Type of claims
 - B. Agency
 - C. From
- То
- D. Approximate number of claims reviewed.
- 4. Availability (Between the hours of 7:00 a.m.-4:30 p.m.)

Approximate hours and days available for case review:

		•			
MON_	 TUE.	 WED	 THU	 FRI	

When addressing availability, please indicate the maximum in terms of *both* days and hours that you would be available if requested by the Social Security Administration.

In addition to the above criteria, the following will be considered for the position of Regional Medical Advisor:

5. Administrative/Management/Leadership Experience

- Experience providing direction to other physicians in medical and program areas.
- B. Experience providing medical guidance to non-medical personnel in the formulation of policy and procedures.
- C. Experience in developing governmental regulations.
- D. Demonstrated leadership in professional organizations.

6. Training of Physicians

- Experience in training physicians in governmental regulations, policies, and procedures.
- B. Other relevant educational/training experience.

Your curriculum vitae and the above information should be sent to:

Contracting Officer Department of Health and Human Services 50 United Nations Plaza, Room 403 San Francisco, CA 94102 (Continued from Page 790)

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FAMILY PRACTICE-GENERAL SURGERY. Multiple practice situation, long established. Prime Orange County, California beach city location. Adjacent to modern hospital with ICU/CCU. Includes equipment, assumable lease. Reply to Number 17, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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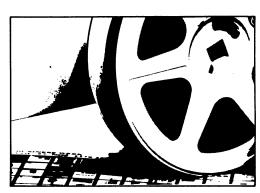






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WYOMING MEDICAL SOCIETY

84th ANNUAL MEETING WMS HOUSE OF DELEGATES AND SCIENTIFIC SESSION JUNE 25-28, 1987 • JACKSON LAKE LODGE, MORAN, WYOMING • GRAND TETON NATIONAL PARK

WMS ANNUAL MEETING AND SCIENTIFIC SESSION

THE LABORATORY'S CONTRIBUTION TO CLINICAL MEDICINE

	THURSDAY, JUNE 25, 1987	10:45 ам	CARL E. SPEICHER, MD
8:00 ам	REGISTRATION/EXHIBITS		Problem Cases Within the Hospital: The Contribution of the Laboratory
8:30 am	WMS HOUSE OF DELEGATES OPENING SESSION	11:30 ам	QUESTION AND ANSWER ROUNDTABLE
10:30 ам	REFERENCE COMMITTEES	11: 4 5 am	Lunch Break
1:15 рм	LEE K. HERMANN, MD WMS President Welcoming Remarks	2:00 рм	THE DOCTORS' COMPANY RISK MANAGEMENT TEAM A Mock Trial
1:30 рм	CARL E. SPEICHER, MD	4:00 рм	Recess Scientific Session
	The Laboratory and the Healthy Patient: What Do We Really Need?	6:00 рм	WMS PRESIDENT'S RECEPTION AND BANQUET MICHAEL J. SULLIVAN
2:15 рм	CARL E. SPEICHER, MD The Outpatient: A Look at the More Common Diagnostic Problems, New Aspects of Laboratory Testing		Governor of Wyoming, Speaker Entertainment and Dancing
3:00 рм	Coffee Break		SATURDAY, JUNE 27, 1987
3:00 РМ 3:15 РМ	JOHN C. NEFF, MD	8:00 ам	REGISTRATION/EXHIBITS
3.13 PM	Infectious Mononucleosis: The Child, the Adolescent and the Adult—Current Concepts	9:00 am	LEE K. HERMANN, MD Introductory Remarks
4:00 рм	QUESTION AND ANSWER ROUNDTABLE	9:00 ам	JOHN C. NEFF, MD
4:30 рм	RECESS SCIENTIFIC SESSION		Hepatitis: Current Applications of the Serologic Markers
6:00 рм	WELCOME TO THE TETONS SOCIAL HOUR (Hosted by The Doctors' Company)	9:45 am	JAMES M. AVENT, MD The Thin Needle: Uses and Abuses
	1 ,,	10:30 ам	Coffee Break
8:00 ам	FRIDAY, JUNE 26, 1987 REGISTRATION/EXHIBITS	10:45 ам	JOHN C. NEFF, MD Let's Look at the Complications of Blood Transfusions
9:00 AM	LEE K. HERMANN, MD	11:30 ам	QUESTION AND ANSWER ROUNDTABLE
	Introductory Remarks	12 noon	Recess Scientific Session Afternoon Free
9:00 ам	ARTHUR E. PELLEGRINI, MD What Is That Funny Looking Pigmented Skin Lesion?	6:00 рм	SOCIAL HOUR
9:45 ам	ARTHUR E. PELLEGRINI, MD Current Therapeutic Approaches to the Aggressive		(Hosted by Capitol Recoveries)
	Melanocytic Tumors		SUNDAY, JUNE 28, 1987
10:30 am	Coffee Break	9:00 am	WMS HOUSE OF DELEGATES CLOSING SESSION

FACULTY

James M. Avent, MD Assistant Professor University of Utah Cytopathologist St. Mark's Hospital Salt Lake City John C. Neff, MD Professor of Pathology Ohio State University Columbus, Ohio Arthur Pellegrini, MD Captain, United States Navy Department of Dermatology United States Naval Hospital San Diego Carl E. Speicher, MD Professor of Pathology Director of Clinical Labs Ohio State University Columbus, Ohio Risk Management Team The Doctors' Company Santa Monica, California



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References:

- 1. Moss SJ: The worldwide decline in caries prevention, in Mead Johnson Clinical Report Series, Clinical Importance of Fluoride Nutrition in Infants, Children, and Young Adults. Chicago, Pragmaton? 1985, Number 1, p. 2.
- 2. Newbrun E: How fluoride works: Topical vs. systemic action, in Mead Johnson Clinical Report Series, Clinical Importance of Fluoride Nutrition in Infants. Children, and Young Adults. Chicago, Pragmaton® 1985, Number 1, p. 5.
- 3. Aasenden R and Peebles T: Effects of fluoride supplementation from birth on human deciduous and permanent teeth. *Arch Oral Biol* 1974;19:321.



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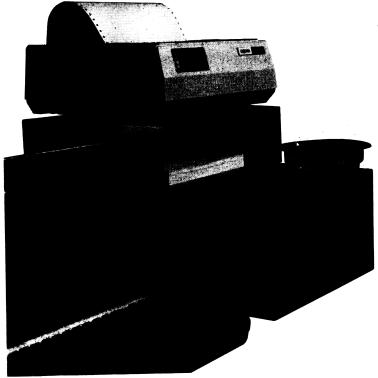


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JULIAN O. NICHOLSON, MD, PRESIDENT IDAHO MEDICAL ASSOCIATION

95th ANNUAL MEETING—IDAHO MEDICAL ASSOCIATION

WEDNESDAY, JULY 29, 1987

9 am to

5 pm HOUSE OF DELEGATES

THURSDAY, JULY 30 SCIENTIFIC SESSION

7:30 am BIOLOGIC CONTROL OF CANCER

John Thompson, MD

University of Washington, Division of Oncology

9:30 am CANCER PAIN

George Khoury, MD

UCLA Cancer Pain Clinic, UCLA Anesthesiology Dept., Los Angeles, California

11:00 am CURRENT STATUS OF VIRUS TREATMENT

Ann Collier, MD

Harborview Medical Center, Seattle, Washington

1:30 pm ALTERNATIVE THERAPIES

Paul Wassermann, MD

Scottsdale Clinic, Division of Oncology

2:30 pm WHERE ARE WE GAINING IN THE BATTLE AGAINST CANCER?

John Thompson, MD

3:30 pm SCREENING FOR CANCER, WHERE DOES IT PAY?

Paul Wassermann, MD

FRIDAY, JULY 31 SCIENTIFIC SESSION

8:30 am ONCOLOGIC IMAGING IN DIAGNOSIS AND STAGING

Charles Carrasco, MD

St. Luke's Hospital, Boise, Idaho

10:00 am MAMMOGRAPHIC SCREENING—IS IT WORTH THE TROUBLE?

Jake Meighan, MD

Inland Imaging, Spokane, Washington

Father Bill Wassmuth, Chairman, Kootenai County Task Force on Human Relations, will address the IMA Auxiliary this morning

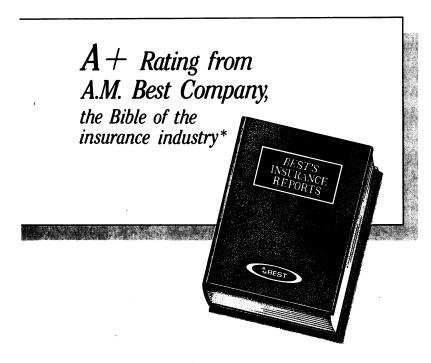
SATURDAY, AUGUST 1

8:30 am CLOSING SESSION, HOUSE OF DELEGATES



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BRIEF SUMMARY OF PRODUCT INFORMATION

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling. INDICATIONS AND USAGE: ZANTAC® is indicated in:

1. Short-term treatment of active duodenal ulcer. Most patients heal within four weeks.

neal within four weeks.

2. Maintenance therapy for duodenal ulcer patients at reduced dosage after healing of acute ulcers.

3. The treatment of pathological hypersecretory conditions (eg, Zollinger-Ellison syndrome and systemic mastocytosis).

4. Short-term treatment of active, benign gastric ulcer. Most patients heal within six weeks and the usefulness of further treatments heal within six weeks and the usefulness of further treatments.

ment has not been demonstrated.

5. Treatment of gastroesophageal reflux disease (GERD). Symptomatic relief commonly occurs within one or two weeks after starting therapy and is maintained throughout a six-week course of ther-

In active duodenal ulcer; active, benign gastric ulcer; hyper secretory states; and GERD, concomitant antacids should be given as needed for relief of pain.
CONTRAINDICATIONS: ZANTAC* is contraindicated for patients

known to have hypersensitivity to the drug.

PRECAUTIONS: Symptomatic response to ZANTAC* therapy does

not preclude the presence of gastric malignancy.

Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see DOSAGE AND ADMINISTRATION). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in

False-positive tests for urine protein with Multistix* may occur during ZANTAC therapy, and therefore testing with sulfos

Although recommended doses of ZANTAC do not inhibit the action of cytochrome P-450 enzymes in the liver, there have been action of cytochrome P-45U enzymes in the liver, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg., a pH-dependent effect on absorption or a change in volume of distribution).

Lack of experience to date precludes recommending ZANTAC for use in children or pregnant patients. Since ZANTAC is secreted in human milk, caution should be exercised when administered to a pursing mother.

a nursing mother

ADVERSE REACTIONS: Headache, sometimes severe, seems to be related to ZANTAC* administration. Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain have been reported. There have been rare reports of malaise, dizziness, somnolence, insomnia, vertigo, tachycardia, bradycardia, prema-ture ventricular beats, and arthralgias. Rare cases of reversible

ture ventricular beats, and arthraighas. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed with or without invention. lar or mixed, with or without jaundice.

There have been rare reports of reversible leukopenia, granulo-

cytopenia, thrombocytopenia, and pancytopenia.

Although controlled studies have shown no antiandrogenic activity, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.
Incidents of rash, including rare cases suggestive of mild ery-

thema multiforme, and, rarely, alopecia, have been reported, as well as rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current

recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particupatient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage

is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison Syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage

is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so the the timing of a scheduled dose coincides with the end of hemodial-

ysis.

HOW SUPPLIED: ZANTAC* 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

ZANTAC* 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Dottles of BU tablets (NDC 01/3-0344-42) and unit dose packs or 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

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Glaxo

Research Triangle Park, NC 27709

Rocephin[®] IV-IM © Ceftriaxone sodium/Roche

Before prescribing, please consult complete product information, a summary or wince notions: MICROBIOLOGY. The bacterical activity of ceftriaxone results from inhibition of cell wall synthesis Ceftriaxone has a high degree of stability in the presence of beta-lactamases, both pencillinases and cephalospornases, of gram-negative and gram-positive bacteria. Ceftriaxone is usually active against the following microorganisms in wino and in clinical infections (see indications and Usage) GRAM-NECATIVE AEROBES: Enterobacter aerogenes, Enterobacter cloacae, Eschenchia coi, Hae-mophilus influenzae (including ampicillin-resistant strains), Hip paranthuenzae, Kribevella species (includ-ing K preumonae). Neissena gonormoeae (including pencilinase and nonpencilinase producing strains), Neissena meningitidis, Proteus mirabilis, Proteus vulgans, Morganella morganii and Serrata macescens:

marcescers

Note: Many strains of the above organisms that are multiply resistant to other antibiotics, e.g., penicilins, cephalosporns and amnoglycosides, are susceptible to cethraxone sodium. Cethraxone is also active against many strains of Pseudomonas aeruginosa.

GRAM-POSITIVE AEROBES: Staphylococcus aureus (including penicilinase-producing strains) and Staphylococcus epidermidis (Note: methicilin-resistant staphylococcus are resistant to cephalospornis, including cethraxone). Streptococcus progress (Group A beta-hemotylis streptococcus agaiactiae (Group B streptococcus progress (Group A beta-hemotylis streptococcus, agaiactiae (Group B streptococcus) are sustant).

Cethraxone also demonstrates in vitro activity against the following microorganisms, although the clinical sontificance is unknown:

significance is unknown
GRAM-NEGATIVE AEROBES. Citrobacter freundli, Citrobacter diversus, Providencia species (including
Providencia retigen), Salmonella species (including S. typhi). Shigella species and Acinetobacter

calcoscercus

ANAEROBES: Bacteroides species, Clostridum species (Note most strains of C difficile are resistant)

SUSCEPTIBILITY TESTING: Standard susceptibility disk method. Quantitative methods that require
measurement of zone diameters give the most precise estimate of antibiotic susceptibility one such
procedure (Bauer MW, Krby WMM, Sherris JC, Türck M, Antibiotic Susceptibility Testing 9.5 standardzed
Single Disk Method, Am J Clin Patriol 45, 493-496, 1996; Standardzed Disk Susceptibility Test, Federal
Register 39 19182, 19184, 1914, National Committee for Clinical Laborationy Standards. Approved Standard ASM 2, Performance Standards for Antimicrobial Disk Susceptibility Tests, July 1975) has been
recommended for use with disks to test susceptibility to effination.

Laboratory results of the standardzed single-disk susceptibility test using a 30-mcg ceftnaxone disk
should be interpreted according to the following three criteria.

1. Susceptible organisms produce zones of 18 mm or greater, indicating that the tested organism is likely.

- 1. Susceptible organisms produce zones of 18 mm or greater, indicating that the tested organism is likely
- Organisms that produce zones of 14 to 17 mm are expected to be susceptible if a high dosage (not to exceed 4 gm per day) is used or if the infection is confined to tissues and fluids (e.g., unne), in which high artibotic levels are attained.
- stant organisms produce zones of 13 mm or less, indicating that other therapy should be selected Organisms should be tested with the ceftriaxione disk, since ceftriaxione has been shown by in vitro tests to be active against certain strains found resistant to cephalosporin class disks.

to be active against certain strains found resistant to cephalosporin class disks. Organisms having zones of less than 18 mm around the cephalothin disk are not necessarily of intermedate susceptibility or resistant to ceffinatione.

Standardized procedures require use of control organisms. The 30-mcg ceffinatione disk should give zone dameters between 29 and 35 mm, 22 and 28 mm and 17 and 23 mm for the reference strains E coli ATCC 25922. Saureus ATCC 25923 and P aeruginosa ATCC 27853, respectively.

DILUTION TECHNIQUES: Based on the pharmacokinetic profile of ceffinatione, a bacterial solate may be considered resistant to ceffinatione in the MIC value for ceffinatione is not more than 16 mcg/mi. Organisms having an MIC value of less than 64 mcg/mi. but greater than 16 mcg/mi, are expected to be susceptible if a high disage (not to exceed 4 gm per day) is used or if the infection is confined to tissues and fluids (e.g., urine), in which high antibotic levels are attained.

E coli ATCC 25922, Saureus ATCC 25923 and P aeruginosa ATCC 27853 are also the recommended reference strains for controlling ceffinatione dilution tests. Greater than 95% of MICS for the E coli strain should fall within the range of 0.016 to 0.5 mcg/mi. The range for the Saureus strain should be 1 to 2 mcg/mi, while for the P aeruginosa strain the range should be 8 to 64 mcg/mi.

INDICATIONS AND USAGE: Rocephin is indicated for the treatment of the following infections when caused by susceptible organisms indicated for the treatment of the following infections when caused by susceptible organisms.
LOWER RESPIRATORY TRACT INFECTIONS caused by Sirep pneumoniae. Streptococcus species (excluding enterococci), Staph aureus, H influenzae, H paramfluenzae, Klebsiella species (including K pneumoniae), E. coli, E. aerogenes, Proteus mirabilis and Serrata marcescens.

preumoniae), E. coit, E. aerogenes, Proteus mirabilis and Seriatia marcescens.

SKIN AND SKIN STRUCTURE INFECTIONS caused by Staph aueus, Staph epidermidis, Streptococcus species (including enterococci), E. cloacae, Klebsiella species (including K. pneumoniae), Proteus mirabilis and Pseudomonias euroginosa.

URINARY TRACT INFECTIONS (complicated and uncomplicated) caused by E. coli, Proteus mirabilis, Proteus wilgaris, M. morgani and Klebsiella species (including K. pneumoniae).

UNCOMPLICATE GONORAPIA (central) quefatrial and rectail) caused by Neissena gonorinoeae, including both penicilinase and nonpenicilinase producing strains.

PSI UNC INFEL ANAMATION (USE-SE Caused by Noncorribose).

including both pericilinase and non-pericilinase producing strains

PELVIC INFLAMMATORY DISEASE caused by N. gonormoeae

BACTERIAL SEPTICEMIA caused by Staph. aureus, Strep. pneumoniae, E. coli, H. influenzae and K.

pneumonae. BONE AND JOINT INFECTIONS caused by Staph aureus, Strep pneumonae. Streptococcus species (excluding enterococci), E coli, P mirabilis, K pneumonae and Enterobacter species INTRA-ABDOMINAL INFECTIONS caused by E coli and K pneumonae. MRNINGITIS caused by H influenzae N memigridis and Strep pneumonae Cettriaxone has also been used successfully in a limited number of cases of meningitis and shunt infections caused by Staph enderometer and E coli. midis and É.coli.

epidermidis and £ coli.

PROPHYLAXIS: The administration of a single dose of ceftnaxone preoperatively may reduce the incidence of postoperative infections in patients undergoing coronary artery bypass surgery.

Although ceftnaxone has been shown to have been as effective as cefazolin in the prevention of infection following coronary artery bypass surgery, to placebo-controlled trails have been conducted to evaluate any cephalosporn antibiotic in the prevention of infection following coronary artery bypass surgery.

SUSCEPTIBILITY TESTING: Before instituting treatment with Rocephin, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug Therapy may be instituted prior to obtaining results of susceptibility testing. CONTRAINDICATIONS: Rocephin is contraindicated in patients with known allergy to the cephalosporin

CUNITIVAINDICATIONS: Rocephin is contraindicated in patients with known allergy to the cephalosporin class of antibolics.

WARNINGS: BEFORE THERAPY WITH ROCEPHIN IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORIMS, PENCALLINGS OR OTHER DRUGS THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENCALLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PRATTICULARLY TO DRUGS SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE THE USE OF SUBCUTANEOUS EPINEPHRINE AND OTHER EMERGENCY MEASURES.

NECUS Enterprising AND UTILE INSTRUCTION TO MEASURES.

Pseudomembranous collis has been reported with the use of cephalosporns (and other broad spectrum antibolics), therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibolic use.

ROCEPHIN® (ceftriaxone sodium/Roche)

Treatment with broad spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by Clostridium difficile is one primary cause of antibiotic associated colitis. Cholestyramine and colestipol resins have been shown to bind to the toxin in vitro.

Mild cases of colitis réspond to drug discontinuance alone. Moderate to severe cases should be man-aged with fluid, electrolyte and protein supplementation as indicated.

when the colitis is not releved by drug discontinuance or when it is severe, oral vancomyon is the treatment of choice for antibotic associated pseudomembranous colitis produced by C difficile. Other causes of collitis should also be considered.

PRECAUTIONS: GENERAL Although transent elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of Rocephin is similar to that of other

cephalosporins. Cettraxone is excreted via both biliary and renal excretion (see Clinical Pharmacology) Therefore patients with renal failure normally require no adjustment in dosage when usual doses of Rocephin are administered, but concentrations of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly.

Dosage adjustments should not be necessary in patients with hepatic dystunction, however, in patients.

with both hepatic dysfunction and significant renal disease. Rocephin dosage should not exceed 2 gm daily without close monitoring of serum concentrations

daily winhout close monitoring of serum concentrations.
Alterations in prothrombin times have occurred rarely in patients treated with Rocephin Patients with
impaired vitamin K synthesis or low vitamin K stores (e.g., chronic hepatic disease and mainutrition) may
require monitoring of prothrombin time during Rocephin trealment Vitamin K administration (10 mg
weekly) may be necessary if the prothrombin time is prolonged before or during therapy.
Prolonged use of Rocephin may result no evergrowth of nonsusceptible organisms. Careful observation of
the patient is essential if superinfection occurs during therapy, appropriate measures should be taken
Rocephin behalf be independent with cauching with a before oil of participation of careful
Rocephin behalf be independent with cauching and the size of a protection of careful
Rocephin behalf be independent with cauching and the size of a protection of careful
results.

Rocephin should be prescribed with caution in individuals with a history of gastrointestinal disease

especially coitis

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY Carcinogenesis. Considering the maximum duration of freatment and the class of the compound carcinogenicity studies with cettriaxone in animals have not been performed. The maximum duration of animal toxicity studies was six months.

in animals have not been performed. The maximum duration of animal toxicity studies was six months Mutagenesis. Genetic toxicology tests included the Ames test, a microniculeus test and a test for chromosomal aberrations in human lymphocytes cultured in wirro with celtriaxone. Celtriaxone showed no potential for mutagenic activity in these studies impairment of Fertiaty. Celtriaxone produced no impairment of Iertiaty when given intravenously to rats at daily doses up to 586 mg/kg/day, approximately 20 times the recommended clinical dose of 2 gm/day. PREGNANCY Featogenic Effects. Pregnancy Category 8 Perfouductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, teletoxicity or teratogenicity in primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately three times the human dose.

approximately lines in less the name to use.

There are, however, no adequate and well controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteralogone Effects In rats, in the Segment I (lertility and general reproduction) and Segment III (pernatal and postnatal) studies with intravenously administered ceftriaxone, no adverse effects were noted on various reproductive parameters during gestation and lactation, including postnatal growth functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less

functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less NURSING MOTHERS. Low concentrations to Certinaxione are excreted in human milk. Caution should be exercised when Roccephin is administered to a nursing woman PEDIATRIC U.SE. Salety and effectiveness of Roccephin in neonates infants and children have been established for the dosages described in the Dosage and Administration section.

ADVERSE REACTIONS: Roccephin is generally well tolerated in clinical trials, the following adverse reactions, which were considered to be related to Roccephin therapy or of uncertain etiology were observed LOCAL REACTIONS—pain, industrial or tendeness at the site of injection (1%) Less frequently reported (less than 1%) was phelotis after IV administration.

HYPERSENSITIVITY—rissh (17%) Less frequently reported (less than 1%) were privritus, fever or chills HEMATO (1000—espencyblast (6%). Intronocyclosis (6.1%) and Lewlooners (2.1%). Less frequently responsed to the propriate of the control of the propriate (less than 1%).

HEMATOLOGIC—eosinophilia (6%), thrombocytosis (51%) and leukopenia (21%). Less frequently reported (less than 1%) were anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the protrombin time.

GASTROINTESTINAL —diarrhea (27%) Less frequently reported (less than 1%) were naus

and dysgedsia

HEPATIC —elevations of SGOT (31%) or SGPT (33%) Less frequently reported (less than 1%) were elevations of alkaline phosphatase and bilirubin

RENAL -elevations of the BUN (12%) Less frequently reported (less than 1%) were elevations of creatinine and the presence of casts in the urine

CENTRAL NERVOUS SYSTEM—headache or dizziness were reported occasionally (less than 1%)

GENITOURINARY—monitiasis or vaginitis were reported occasionally (less than 1%)

MISCELLANEOUS - diaphoresis and flushing were reported occasionally (less than 1%)

MISCELLANEOUS—daphoress and flushing were reported occasionally (less than 1%) of the rarely observed adverse reactions (less than 0.1%) include leukocytosis. lymphocytosis mono cytosis basophilia, a decrease in the prothrombin time, aundice glycosuria hematuria, bronchospasm serum sickness, abdomnal pain, colitis, flatulence dyspepsia, palpitations and epistaxis. DOSAGE AND ADMINISTRATION: Rocephin may be administered intravenously or intramuscularly. The usual adult daily doses is 1 to 2 gm given once a day (or in equally divided doses twice a day) depending on the type and severify of the infection. The triot daily dose should not exceed 4 grams. For the treatment of serious miscellaneous infections in children, other than meninghis, the recommended total daily dose is 50 to 75 mg/kg (not to exceed 2 grams) given in divided doses every 12 hours. Generally, Rocephin therapy should be continued for at least two days after the signs and symptoms of infection have disappeared. The usual duration is 4 to 14 days, in complicated infections longer therapy may be required.

In the treatment of meningitis, a daily dose of 100 mg/kg (not to exceed 4 grams), given in divided doses every 12 hours, should be administered with or without a loading dose of 75 mg/kg. For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is

For preoperative use (surgical prophylaxis), a single dose of 1 gm administered ½ to 2 hours before

When treating infections caused by Streptococcus pyogenes, therapy should be continued for at least

No dosage adjustment is necessary for patients with impairment of renal or hepatic function, however, blood levels should be monitored in patients with severe renal impairment (e.g., dialysis patients) and in patients with both renal and hepatic dysfunctions.

HOW SUPPLIED: Rocephin (ceftriaxone sodium/Roche) is supplied as a sterile crystalline powder in glass vials and piggyback bottles. The following packages are available.

Vials containing 250 mg equivalent of ceftriaxone. Boxes of 10 (NDC 0004 1962 01)

Vals containing 250 mg equivalent of cettraxone Boxes of 10 (NDC 0004 1962 01)
Vals containing 500 mg equivalent of cettraxone Boxes of 10 (NDC 0004 1963 01)
Vals containing 1 gm equivalent of cettraxone Boxes of 10 (NDC 0004 1964 01)
Vals containing 2 gm equivalent of cettraxone Boxes of 10 (NDC 0004 1964 03)
Vals containing 2 gm equivalent of cettraxone Boxes of 10 (NDC 0004 1965 01)
Piggyback bottles containing 2 gm equivalent of cettraxone Boxes of 10 (NDC 0004 1965 03)
Bulk pharmacy containers, containing 10 gm equivalent of cettraxone Boxes of 10 (NDC 0004 1971 01)
NOT FOR DIRECT ADMINISTRATION

Roche Laboratories Division of Hoffmann-La Roche Inc.

Nutley, New Jersey 07110









The one antimicrobial that belongs on every formulary.

Once-a-day ROCEPHINOM Ceftriaxone sodium/Roche

* ROCEPHIN is indicated in the following infections: bacterial septicemia, bone and joint, intra-abdominal, lower respiratory tract, skin and skin structure, urinary tract, bacterial meningitis and gonorrhea. Please see summary of product information on adjacent page for indicated susceptible organisms.